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UTERINE CONTRACTIONS IN NORMAL AND ABNORMAL LABOUR

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WHEN prolonged and difficult labour occurs in the absence of disproportion, malpresentation or malposition, it is attributed to faults in the forces, usually called "uterine dysfunction". Murphy (1947), Reynolds (1951), Caldeyro Barcia and Alvarez (1952), Williams (1952), Alvarez and Caldeyro Barcia (1953) and many others have claimed that in normal labour the contractions are regular and well co-ordinated; the stronger the contractions, the quicker the labour. When labour is prolonged, in the absence of disproportion, they are said to be irregular and inco-ordinated or weak and infrequent.

This may seem logical but in practice it does not always fit the clinical facts. Labour is sometimes quick and easy despite irregular uterine contractions or may be prolonged and difficult even with strong and regular contractions. Undue resistance of the cervix—"cervical dystocia"—is said to be the primary factor in some cases; in these the head may be deep in the pelvis and the cervix well thinned out, but there is little dilatation. According to Jeffcoate, Baker and Martin (1952), this clinical picture is rare.

Nevertheless, as is well known, labour in multiparae is usually shorter and easier, and more often ends spontaneously than in primiparae, unless previous births have been by Caesarean section before the cervix reached half dilatation. This suggests that the first labour, by stretching the cervix and thus lessening its resistance to subsequent stretching, renders it more easily dilated in a second labour.

Clinically, it is very difficult to say whether any particular difficult labour is primarily due to undue resistance of the cervix or to disordered uterine contractions. Very prolonged labour due to disordered uterine action of all kinds is comparatively uncommon in very young primigravidae, but increases with age (Baird, 1952a, 1952b; Stewart and Scott, 1953; Stewart and Bernard, 1954). The incidence is increased when there is even slight disproportion or when the head is lying in the occipito-posterior position. Any study of uterine action in labour must therefore take account of age and parity, the size of the foetus in relation to the pelvic capacity, and the position of the head.

In this investigation the strength and pattern of the uterine contractions have been recorded in normal and in abnormal labour with and without disproportion by means of a catheter inserted into the uterine cavity.

METHODS

Seventy-five patients (54 primiparae and 21 multiparae) were investigated. In all, the foetus presented by the vertex and weighed more than 5½ pounds (2·5 kg.).

Clinical Classification of Labour

The first stage of labour was considered "normal" when there was no evidence of disproportion and the cervix dilated progressively. Cases where the occiput was posterior were included if the above criteria were satisfied. The second stage of labour was considered normal

when there was no evidence of any mechanical difficulty and delivery was spontaneous, with the occiput anterior. No time factor was used in defining "normal" labour but in fact delivery occurred within 24 hours of the onset of painful contractions in all cases so graded.

Cephalo-pelvic disproportion was diagnosed clinically and confirmed by X-ray pelvimetry when necessary. In the absence of disproportion, the first stage of labour was considered abnormal if the state of the cervix remained unchanged for 2 hours or more. In all cases, the degree of cervical dilatation was personally assessed at intervals by rectal or vaginal examination. In abnormal labours, the classification of Stewart and Bernard (1954) was used to describe the type and degree of difficulty.

Recording of Uterine Contractions

Pressure changes in the amniotic sac have been shown to be a sensitive and accurate index of overall uterine activity during labour (Caldeyro Barcia, Alvarez and Reynolds, 1950). In this study they were recorded by the method described by Williams and Stallworthy (1952). To ensure that tracings from different patients were comparable, care was taken to keep the manometer at the same level relative to the patient in each case. A kymograph capable of recording continuously for 72 hours was used. Tracings were begun as soon as possible after the patient's admission to the labour room and continued until the baby was born. In some prolonged labours, tracings were begun only when the state of the cervix was known to have been unchanged for several hours.

The disadvantages of this method are that occasionally the polythene cannula becomes blocked by vernix, mucus, meconium or blood clot, or that recordings may be unsatisfactory or impossible if all the liquor escapes from the uterus. In the second stage of labour, the cannula may descend with the foetal head so that one or more of the holes in its distal end lie in the vagina.

Measurement of Uterine Contractions Recorded

The mean pressure exerted by the uterus has been used to measure the average strength, duration and frequency of the contractions, and the "resting tone" between them. It is calculated by measuring the area between the tracing and the base line (zero pressure) by a planimeter and dividing the result by the length of the tracing. Figure 1 shows part of the tracings made during the first stage in 2 normal labours. In the first

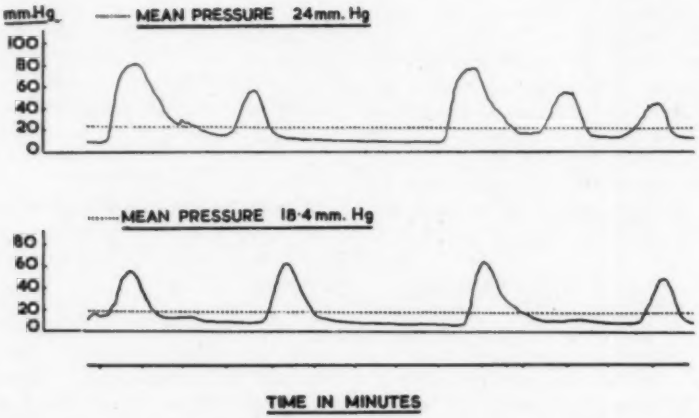

FIG. 1

Sections of Amniotic Pressure Tracings from 2 cases in normal first stage of labour, with Mean Pressure level superimposed in both.

the mean pressure is 24 mm. of mercury and in the second 18·4 mm. In the second stage, the mean pressure includes that resulting from the patient's voluntary expulsive efforts as well as from uterine contractions. In normal labours, the mean pressure was measured throughout the whole length of the tracing in both the first and second stages. In prolonged labours, the average of mean pressures measured over several lengths of the tracing was taken, none of the lengths representing less than 1 hour's continuous recording.

During continuous recordings, the pattern of the contractions changes when the patient shifts her position. Williams (1952) noticed that the contractions became stronger when the patient sat up. In this study, it was found that when the patient was in the left or right lateral position, the contractions were stronger but less frequent than they were when she lay flat on her back. This change in the pattern had no significant effect on the trend of the mean pressure in individual cases, provided the height of the manometer was adjusted when the patient changed position. Later, it was found easier to note the effects of changes of posture at the beginning of a tracing and make the necessary adjustments in measurements when it had been completed, rather than to move the manometer at intervals throughout labour.

The mean pressure indicates the amount of "activity" in the uterus but gives no information about the co-ordination of its action, for it cannot differentiate between regular and irregular contraction patterns. Since peak pressure, duration and frequency of contractions may all vary, and since the "shape" of individual contractions may differ greatly from the normal type shown in Figure 1, it is extremely difficult to devise any precise measurement of regularity. It is possible, however, to classify the pattern of contractions into three main groups by inspection. Figure 2 shows examples of the 3 types of pattern, which have been defined as follows:

Type I. Contractions are regular in strength, frequency and form; any variations in the pattern are slight or occasional.

Type II. Contraction pattern shows some irregularity in strength and frequency, or abnormal contraction forms recur at intervals.

Type III. The pattern is completely irregular and most of the contractions are of abnormal type. Although the "resting tone" is usually within normal limits, the uterus may feel tense because the abnormal contractions are prolonged and last as long as 2 to 6 minutes.

Types II and III correspond approximately to the "first and second degree inco-ordination" described by Alvarez and Caldeyro Barcia (1954).

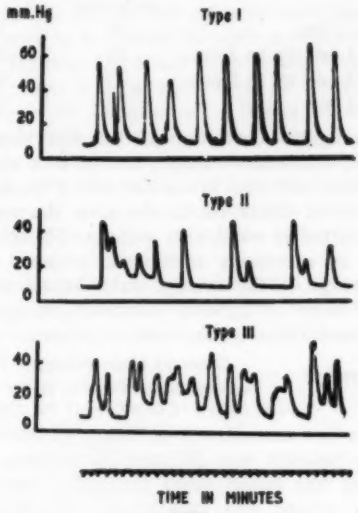

FIG. 2

Sections of tracings from 3 cases in first stage of labour illustrating features of Type I, II and III contractions.

FINDINGS

Uterine Contractions in Normal First Stage of Labour

Primiparae. Tracings have been made in 31 cases of normal labour. The pressure at the peak of contractions was most often between 40 and 60 mm. of mercury, although the range was from 20 to 80 mm. The pressure between contractions, the "resting tone", was usually between 8 and 12 mm., but even in individual cases fluctuated between 6 and 16 mm. These findings are similar to those of other workers. The mean

pressure varied from 15 to 30 mm. of mercury, the average value being 21 mm.

Since the uterine contractions tend to become stronger and more frequent as the first stage of labour progresses, the level of the mean pressure was found to be related to the degree of dilatation of the cervix at the time the pressure record was started, as follows:

Cervical Dilatation when Tracing Started	Average Mean Pressure (mm. of mercury)	Number of Cases
Up to 1 cm.	19	3
Over 1 and up to 3 cm.	20	12
Over 3 and up to 5 cm.	22	9
Over 5 cm.	24	7

These figures show that in the first stage of labour, the mean pressure in one case can be compared with that in another only if the degree of cervical dilatation at the time the tracing was started is taken into account. This can be done by expressing each mean pressure as a percentage of the average value found at the same stage of cervical dilatation to give a "Pressure Index", calculated as follows:

$$\text{Pressure Index} = \frac{\text{Observed Mean Pressure} \times 100}{\text{Average Mean Pressure at the same stage of dilatation of the cervix}}.$$

In the first case shown in Figure 1, where the mean pressure was 24 mm. of mercury, the tracing was begun when the cervix was only partly effaced and not dilated. The pressure index is therefore $\frac{24}{19} \times 100 = 126$, indicating that pressure was 26 per cent above the average. In the second case, where the mean pressure was 18·4 mm., the cervix was 3 cm. dilated when the tracing was begun, therefore the pressure index is $\frac{18 \cdot 4}{22} \times 100 = 92$, indicating that pressure was 8 per cent below the average.

The "Pressure Index" has been used to express the amount of uterine "activity" in the first stage of labour in all cases studied in this paper.

In the 31 normal cases the duration of the first stage ranged from 3 hours to 22 hours 20 minutes, average 12 hours 10 minutes, and the pressure index from 80 to 128, average 101. Type I contractions occurred in 9 cases, Type II in 19 and Type III in 3, the average pressure indices in cases of each type being 110, 95 and 101 respectively. Although Type I contractions were the most powerful, the average length of the first stage for this group was 12 hours 36 minutes, compared with 12 hours 30 minutes for Type II, and only 8 hours 23 minutes for Type III—the type usually considered to be associated with prolonged labour. In fact, no relationship could be found between the pressure index or the regularity of the contractions and the duration of the normal first stage of labour.

The Pressure Index was not related to the weight of the baby, the period of gestation, the age of the mother or the position of the vertex.

Regular contractions occurred most often in cases where the infant weighed less than 7 pounds. Type I contractions were found in 4 of 9 such cases (average birth weight 6 pounds 3 ounces), in 4 of 14 cases with infants between 7 and 8 pounds (average 7 pounds 7 ounces) and in 2 of 8 over 8 pounds (average 8 pounds 11 ounces).

The period of gestation may also affect the contraction pattern, for regular contractions occurred more often in labour occurring before the estimated date of delivery (average 39·5 weeks) than after it (average 41·4 weeks). This difference, however, seemed to be due largely to differences in the size of the infants in the 2 groups, for if only cases with infants over 7 pounds are compared, the contraction patterns before and after term are similar. Since all "normal" cases studied were delivered between 39 and 42 weeks of gestation, a more comprehensive sample would be required to show if the duration of pregnancy does affect the uterine contractions independently of the size of the foetus.

Maternal age was related to the contraction pattern, for Type I contractions were found in 7 of 19 patients under 25 years (average age 20 years), and in only 3 of 12 patients over 25 years (average age 30 years). This difference could not be explained by differences in the baby weights in the two groups, for in cases where the infants were over 7 pounds Type I contractions occurred in 4 of 12 young women, and in 2 of 10 in the older group.

The position of the vertex seemed to have no effect on the contractions, for cases with occipito-anterior, lateral and posterior positions all had similar contraction patterns.

Although the age of the mother and the weight of the baby seemed to affect the regularity of the contractions, they had no accompanying effect on the duration of the normal first stage of labour. Therefore, when contractions in one group of cases are compared with those in another (for example, normal and prolonged labour) one must be sure that any difference found is not due simply to differences in maternal age or baby weight in the two groups.

Multiparae. Tracings were made in 11 multiparae who had a normal first stage of labour. All had been delivered vaginally in previous confinements. The pressure at the peak of contractions was most often between 20 and 40 mm. of mercury, although the range was from 15 to 60 mm. It was thus lower than that in primiparae. The resting tone was similar to that found in first labours (8 to 12 mm. of mercury), but showed less fluctuation. The contractions were usually more frequent than those found in first labours.

The pressure index ranged from 47 to 97, average 66; in only 2 cases was it higher than the lowest recorded in normal primiparae (80). Type I contractions occurred in 7 cases and Type II in 4, none being of the very irregular Type III variety. The length of the first stage varied from 4 hours 50 minutes to 14 hours 50 minutes, average 8 hours 26 minutes. There was no relationship between the pressure index or the contraction pattern and the length of the first stage of labour.

It is obvious that the first stage of labour in multiparae is shorter than in primiparae despite the fact that the pressure index is usually much lower. The shorter first stage in multiparae did not seem to be related to more regular contraction patterns, for it was slightly longer in those with Type I than with Type II contractions (8 hours 44 minutes and 7 hours 55 minutes respectively).

The differences between contractions in multiparae and primiparae were not related to differences in maternal age or baby weight, for, on the average, the multiparae were older and had heavier babies.

Figure 3 illustrates the difference between the contractions in primiparae and multiparae in both first and second stages of labour. The

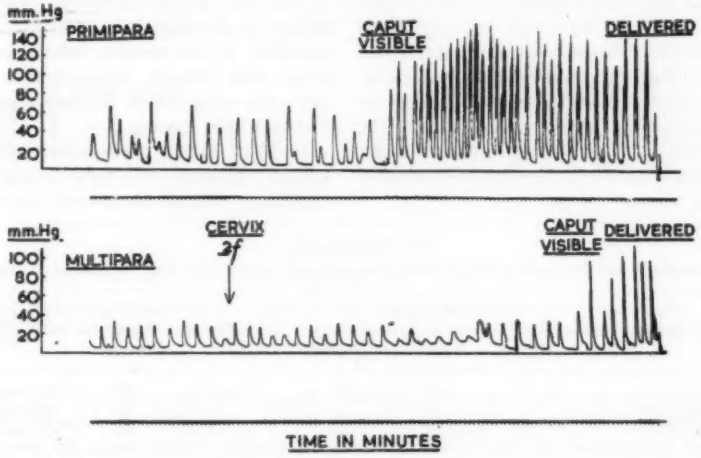

FIG. 3

Tracings from a first and a third labour showing the effect of parity on the amniotic pressure in the first and second stages of labour.

findings in the second stage are described later.

Uterine Contractions in Prolonged First Stage of Labour without Disproportion

Primiparae. Tracings have been made in 19 cases, of which 4 were graded as "Slow Starters", 9 as "Minor Dysfunction" and 6 as "Major Dysfunction" (Stewart and Bernard, 1954). The peak pressures were similar to those found in normal labours, being most often between 30 and 60 mm. of mercury, and occasionally as low as 20 or as high as 80 mm. However, high pressures were less common and the frequency of contractions was often lower than in normal cases. The level of the resting tone was similar to that found in normal labour, being most often between 8 and 12 mm. and ranging from 6 to 16 mm. No case was found where the resting tone was persistently raised to about 20 mm., the pressure said to occur in "hypertonic inertia". The characteristics of "hypotonic inertia", infrequent contractions of normal pattern, and peak pressures of less than 20 mm. of mercury, were found only in one case. Even in this case, the pattern became very irregular after a short time.

Irregular Type III contractions were found more often than in normal labour, but were less common than had been expected. Table I shows that in both the normal and the prolonged labour group about 60 per cent of cases fall into Type II but that the normal group contains about twice the percentage of Type I cases as the abnormal group, while with Type III the position is reversed. The average pressure index in the prolonged labour group was 91 compared to 101 in the normal group.

Compared with the normal group, the women in the abnormal group were older (13 of 19 were over 25 years of age instead of 12 out of 31) and had heavier infants (17 of 19 were over 7 pounds instead of 22 out of 31). When women over 25 years of age delivered of infants over 7 pounds were considered, the differences between the pressure index and the type of contractions in the normal and abnormal groups persisted.

Nevertheless, the differences between the contractions in normal and prolonged first stages seem hardly sufficient to account for the great difference in the duration of the first stage of labour in the two groups. Furthermore, the type of tracing by itself is of little value in predicting the course of labour either in individual cases or in certain groups of cases. Figure 4 shows tracings made during the first stage of labour in 4 primiparae where there was no evidence of disproportion. The 2 upper tracings show regular Type I contractions. In the first case, labour lasted 36 hours because of uterine dysfunction and was ultimately terminated by forceps delivery before the cervix was fully dilated, because of severe maternal distress. In the second case, labour lasted 14 hours and delivery was spontaneous. The two lower tracings show irregular Type III contractions. In the first, labour lasted 69 hours because of severe dysfunction and forceps delivery was required. In the second, labour lasted only 12 hours and delivery was spontaneous. In each case, the contraction pattern shown is typical of the whole tracing.

In 15 of the 19 cases where labour was prolonged because of dysfunction the cervix ultimately dilated completely. In none of these

TABLE I

Pressure Index and Type of Contractions in Prolonged and Normal First Stage of Labour in Primiparae

Type of Labour	Contractions			Total	Average Pressure Index	Average Length of First Stage
	Type I	Type II	Type III			
"Slow Starters"	1	2	1	4	99	37 hours 10 minutes
"Minor Dysfunction" ..	1	6	2	9	89	30 hours 50 minutes
"Major Dysfunction" ..	1	3	2	6	90	65 hours 54 minutes
All abnormal	3	11	5	19	91	43 hours 8 minutes
All normal	9	19	3	31	101	12 hours 10 minutes

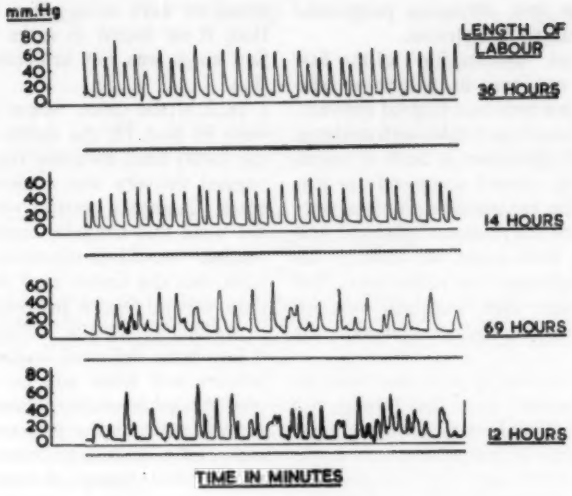

FIG. 4

Sections of tracings from 4 cases in first stage of labour showing that the pattern of contractions does not indicate the rate of progress.

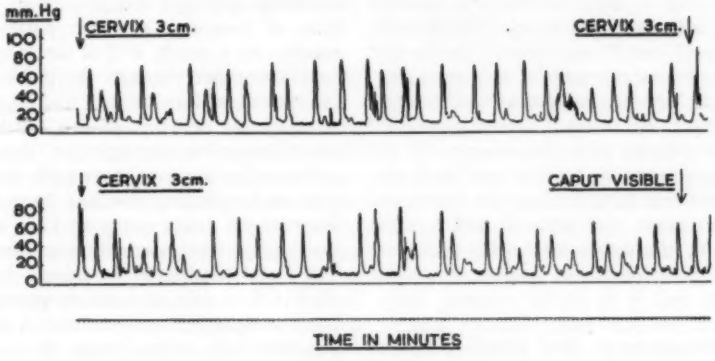

FIG. 5

Two sections of the tracing in a prolonged first stage of labour in a primipara, showing sudden increase in rate of cervical dilatation without any accompanying change in uterine contractions.

cases was there any obvious associated change in the pattern, strength or frequency of the contractions, even in those cases where the eventual speeding up of labour was sudden and dramatic. Figure 5 illustrates this in the case of a primigravida whose labour lasted for 37 hours. In the 2 tracings shown, the contractions are of similar strength and frequency and both have been graded Type II. During the first tracing, the dilatation of the cervix remained unchanged at 3 cm., as it had been for 17 hours previously. During the second tracing, which is a direct

continuation of the first, dilatation progressed smoothly from 3 cm. to completion.

Multiparae. Severe "dysfunction" in the first stage of labour is very rare in multiparae who have had at least one previous vaginal delivery. Tracings have been made in 2 cases with evidence of delay in cervical dilatation in both of which the cervix eventually dilated completely in just under 20 hours. The contraction patterns were Types III and II, and the pressure indices 68 and 55 respectively. In both cases, the state of the cervix remained unchanged for some hours, but progressive dilatation then occurred without any change in the contraction patterns or pressure indices.

When Caesarean section is performed because of "uterine dysfunction" in a first labour, the cervix often fails to dilate beyond the same point in subsequent labours. Tracings have been made in 2 multiparae where the first labour was terminated by Caesarean section for dysfunction. The tracings resemble those found in *first labours*. In both, the contraction pattern was Type I, the pressure at the peak of contractions between 40 and 60 mm. of mercury, and the resting tone between 8 and 10 mm. The pressure indices were 92 and 83 respectively. In the first case, where Caesarean section had been performed in the previous labour when the cervix was two-thirds (7 cm.) dilated, labour progressed quickly and delivery was spontaneous. In the second case, Caesarean section had been performed in the first labour when the cervix was only 3 cm. dilated, and after 30 hours in the second labour the cervix was again dilated to only 3 cm. and Caesarean section was again required.

Uterine Contractions in First Stage of Labour Complicated by Disproportion

Tracings have been made in 9 cases, 4 primiparae and 5 multiparae, where there was some degree of cephalo-pelvic disproportion in the first stage of labour, due mainly to a contracted pelvic brim in each case.

Primiparae. The pattern of contractions was regular, Type I, in only 1 case and very irregular, Type III, in the other 3. The pressure index was 95 in the case with regular contractions, and 54, 64 and 72 in the others. Thus, the contractions were more often irregular and weak than those found in cases where a prolonged first stage was not associated with disproportion.

In 2 of the cases, where the pressure indices were 95 and 72, the cervix dilated completely, the foetal head moulded through the brim, and vaginal delivery was achieved. In the other 2 cases, Caesarean section was required. Despite the weak and irregular contractions, the cervix reached two-thirds dilatation (7 cm.) quickly in both, but the foetal head failed to engage and there was no further progress.

Multiparae. Of the 5 multiparae investigated, 4 had been delivered vaginally in all previous labours and these will be considered first. In one the contraction pattern was of Type III throughout and the pressure index was 70. In each of the other 3, by contrast, the contractions were, at first, typical of those found normally in multiparae, with a regular pattern and peak pressures not higher than 30 mm. of mercury. During this phase, the foetal head remained high and mobile. The contractions then became progressively stronger, reaching peaks of 60 or 70 mm. of mercury, and the pattern remained regular. As a result, in 2 of the cases, the foetal head descended through the pelvic brim when the cervix had fully dilated, and labour ended in spontaneous delivery. In the third case, there was considerable disproportion; the contractions continued to increase in strength and frequency, with peak pressures reaching 70 to 80 mm. and the pressure index rising to 121—almost twice the average level normally found in multiparae. The foetal head failed to engage, however, and after a time, the contraction pattern began to show evidence of inco-ordination and the peak pressures fell, ranging from 20 to 40 mm. of mercury. Caesarean section was performed. Figure 6 shows sections of the tracing in this case to illustrate the sequence of events.

In the fifth multipara in this group, the tracing was made in the second labour. Caesarean section had been required in the first labour because of dystocia associated with disproportion. The labour had been terminated when the cervix was half (5 cm.) dilated. On this occasion, the contraction pattern was Type III. The peak pressures were stronger than those

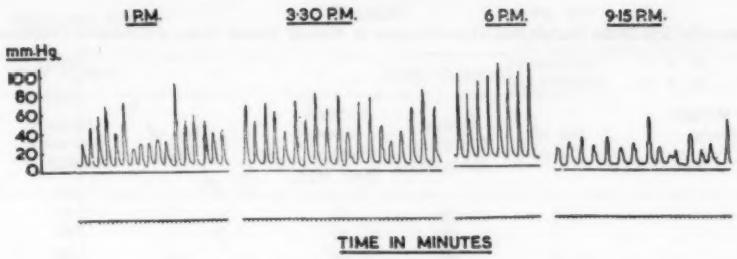

FIG. 6

Four sections of the tracing in a multipara where first stage of labour complicated by severe disproportion. Previous labour normal, with spontaneous delivery. Tracings show contractions gradually increasing in strength but ultimately becoming weak and rather irregular when disproportion could not be overcome. Caesarean section required.

normally found in multiparae, ranging from 30 to 60 mm. of mercury—they were, in fact, similar to those found in primiparae, or to those in multiparae where the previous labour had been terminated by Caesarean section for prolonged labour without disproportion. In this case, Caesarean section was again required, for the foetal head remained high and the cervix dilated no further than it had done in the first labour.

Uterine Contractions in Normal Second Stage of Labour

Primiparae. Tracings of the whole of the normal second stage of labour were made in 30 cases. In 20 of these, the preceding first stage had been normal and in 10 it had been prolonged in the absence of disproportion. There was no significant difference between the tracings in the second stage in the two groups. Figure 3 shows the typical appearance of tracings in the second stage of labour, in which the voluntary expulsive efforts appear as several relatively short "spikes" of very high pressure superimposed on the curve of uterine pressure. As a result, peak pressures were high, being most often between 140 and 160 mm. of mercury, and ranging from 80 to 220 mm. The resting tone was usually higher than it had been in the first stage of labour, being most often between 12 and 16 mm., but ranging from 8 to 20 mm. This increase in the resting tone did not appear to be due to a change from the lateral to the dorsal position, for it often occurred when there had been no change in position. The contraction pattern appeared to be more regular in the second stage of labour than in the first, even in cases where the pattern had previously been Type III. There was no steadily increasing gradient of pressure like that in the first stage, so that the mean pressure, which included the pressure effects of the patient's expulsive efforts, measured the "forces" accurately without further correction. In the 30 cases, the mean pressure ranged from 27 to 71 mm. of mercury and the average was 39 mm. The duration of the second stage ranged from 15 to 128 minutes, and the average was 49 minutes.

No clear relationship could be demonstrated between the level of the mean pressure and the duration of the normal second stage in primiparae. For example, the mean pressure in the shortest second stage (32 mm. of mercury) was the same as that in the longest. In most cases, peak pressures increased at first, as the patient's efforts became more efficient and better co-ordinated but later they began to decrease again, partly because of fatigue and partly, perhaps, because of apprehension when the foetal head began to distend the perineum. Mean pressures were therefore slightly lower in the longer second stages, but this seemed to be an effect, rather than a cause, of the delay.

The factors which most affected the duration of the second stage in these cases were the age of the mother and the weight of the baby. Neither the period of gestation nor the position of the vertex in the first stage of labour had

TABLE II

Maternal Age, Baby Weight and Mean Pressure in Normal Second Stage of Labour in Primiparae

Baby Weight (Pounds)	Under 25 Years			Over 25 Years		
	No. of Cases	Average Duration (minutes)	Average Mean Pressure (mm. Hg)	No. of Cases	Average Duration (minutes)	Average Mean Pressure (mm. Hg)
Under 7	6	28	41	3	55	42
7–8	8	42	41	5	61	35
Over 8	4	40	38	4	83	36
Total	18	37	40	12	67	37

any significant effect. (One case, where spontaneous "face-to-pubes" delivery occurred, was excluded from this "normal" group.)

Table II shows the effects of maternal age and baby weight in the second stage in these primiparae. In cases where the infants are of similar weight, the second stage tends to be longer in the older than in the younger women. In women of similar age, it tends to increase in length with the weight of the baby.

Multiparae. Tracings were made in 13 multiparae who had a normal second stage of labour. In comparison with primiparae, the peak pressures were usually low, being most often between 60 and 100 mm. of mercury, but ranging from 40 to 160 mm. The resting tone was usually between 8 and 12 mm. but in 4 cases it was as high as 14 to 18 mm. The mean pressure ranged from 16 to 45 mm. and averaged 30 mm. The duration of the second stage ranged from 4 to 36 minutes, and averaged 16 minutes. As in primiparae, no relationship could be demonstrated between the level of the mean pressure and the duration of the second stage. The number of cases in this group was too small for the effects of maternal age and baby weight to be assessed in detail. However, the second stage in the multiparae was much shorter than that in the primiparae although the mean pressure was lower, despite the fact that the multiparae were, on the average, older and had bigger babies.

Uterine Contractions in Abnormal Second Stage of Labour

The number of cases in this group was small. In primiparae, there was delay in the second stage, due to a minor degree of disproportion in 4 cases, and in the absence of any mechanical factor in 2. There was no significant difference between the tracings in these cases and those where the second stage was normal. In the 2 cases where delay was attributed clinically to "dysfunction", the peak pressures were between 130 and 160 mm. of mercury, and the mean pressures were 37 and 42 mm. of mercury. In multiparae, there was evidence of slight disproportion in the second stage in 2 cases. In both, peak pressures were high (140 to 160 mm.) and delivery spontaneous.

DISCUSSION

It is clear that the rate of progress in labour cannot be related simply and directly either to the strength or to the regularity of the uterine contractions.

Figure 7 shows, in a scatter diagram, the length of the first stage of labour, the pressure index and the type of contractions in the 63 primiparae and multiparae where there was no disproportion. There is no evidence that the duration of the first stage is in any way associated with the pressure exerted by uterine contractions, and the type of contractions is obviously not of decisive importance; indeed, the most obvious feature is that most multiparae had shorter labours as well as much lower pressures than most primiparae. Figure 8 shows, in similar fashion, the length of the second stage of labour and the mean pressure in the 43 primiparae and multiparae where there was no mechanical

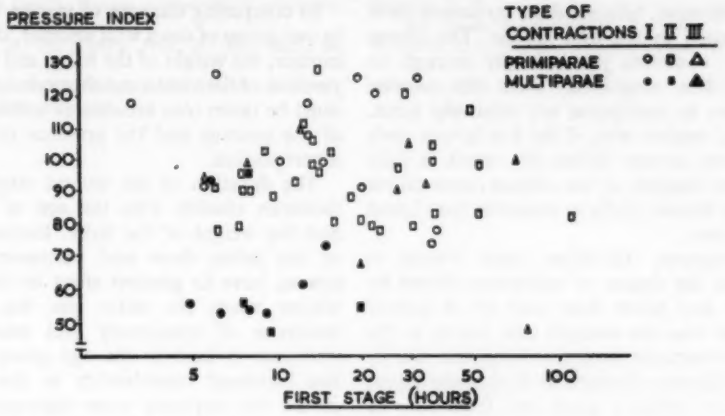

FIG. 7

The relationship between Pressure Index and type of contractions and the length of the first stage of labour in 63 cases uncomplicated by disproportion.

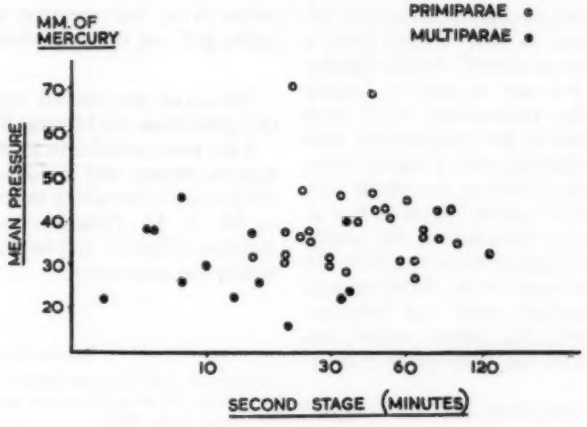

FIG. 8

The relationship between Mean Pressure and duration of the second stage of labour in 43 cases uncomplicated by disproportion.

difficulty in the second stage and delivery was spontaneous. Again the effect of parity is obvious—lower pressures are associated with faster progress in multiparae compared with primiparae. But in neither group is the duration of the second stage related to the level of the mean pressure.

The effect of parity in speeding up labour is almost certainly that the degree of resistance of the cervix and pelvic floor to stretching is much

less in multiparae, because these structures have been stretched in the first labour. The uterus apparently contracts just strongly enough to overcome this resistance. Thus the uterine contractions in multiparae are relatively weak. This would explain why, if the first labour ends in Caesarean section before the cervix is fully dilated, the strength of the uterine contractions in the next labour tends to resemble that found in primiparae.

In primiparae, therefore, once labour is established, the degree of resistance offered by the cervix and pelvic floor may be of greater importance than the strength and nature of the uterine contractions in determining the rate of progress of labour. It seems likely that the degree of resistance varies a good deal from case to case: a low resistance would explain why labour can progress quickly and easily despite weak and irregular contractions and a high resistance why labour can be prolonged despite strong regular contractions.

In multiparae, the uterus does not normally have to contract very strongly to overcome the low tissue resistance, so that it must have a considerable "reserve of power". In the presence of disproportion, this can be used to increase the strength of the contractions to a level similar to that found in first pregnancies, with the result that the disproportion is usually overcome. In primiparae, however, the uterus may have little "reserve of power" since it has to overcome the greater resistance of the cervix. Consequently when disproportion is added, the uterine contractions may not be strong enough and may soon become weak and irregular. Even in multiparae, the uterine action can become disordered if the disproportion is insuperable.

This raises the possibility that the irregular and sometimes weaker contractions seen in prolonged labour without disproportion may not be the primary cause of the prolonged labour but the result of a very high tissue resistance. Similarly, in a prolonged second stage of labour, lower pressures found in such cases may be due to the patient getting tired, and may not be the primary cause of the delay. Again undue resistance of the pelvic floor and the perineum may be the primary cause.

In comparing the type of uterine contractions in one group of cases with another, the age of the mother, the weight of the baby, and possibly the position of the vertex and the period of gestation, must be taken into account as well as the parity of the patients and the presence or absence of disproportion.

The duration of the second stage of labour increases steadily with the age of the mother and the weight of the baby. Increased rigidity of the pelvic floor and perineum would, of course, have its greatest effect on the course of labour when the baby was big. Since the incidence of episiotomy and tearing of the perineum is least in the age group 15–19 and has increased considerably in the age group 20–24, this increased tissue resistance may start at a surprisingly early age (Baird, 1952a, 1952b). The fact that, in the absence of disproportion, prolonged first or second stages of labour are almost confined to primigravidae, suggests that the stretching of the birth canal, by greatly lowering the resistance of the cervix and the pelvic floor, has removed the chief cause of prolonged and difficult labour.

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IN VITRO STUDIES OF THE MOTILITY OF THE HUMAN UTERUS

Part I—The Spontaneous Motility in Different Parts of the Non-pregnant Uterus During the Sexual Cycle and in the Menopause and Its Correlation with the Actomyosin Content

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IN previous investigations concerning the motility of the human uterus *in vitro* the site of origin of the muscle strips used in the experiments has not been strictly defined. This fact might possibly explain the varying results reported (Kehrer, 1907; Runge, 1929; Adair and Haugen, 1939; Del Sol Fernandez, 1951).

In a paper (Ingelman-Sundberg, Lindgren, Rydén and Sandberg, 1954) we published some preliminary results from an investigation with well-defined muscle strips studied *in vitro* using the Magnus-Kehrer technique.

We were able to state that strips taken from the isthmus region demonstrated a sphincter-like motility pattern. These investigations have now been carried out on a larger material and have been completed by determination of the actomyosin and myosin content.

MATERIAL AND METHODS

Material. The muscle strips were taken from uteri of women operated upon for uterine fibroids. Immediately after hysterectomy muscle strips from an intermediate layer were cut longitudinally and transversely from the following locations: (1) uterine cornua, (2) corpus, (3) isthmus and (4) cervix. The strips were then immersed in Ringer solution.

Motility. As soon as possible the muscle strips, measuring about 20×2×2 mm., were immersed in an organ-bath containing Tyrode solution, modified according to Genell (1937) and oxygenated by a gas mixture containing 95 per cent O_2 and 5 per cent CO_2. After a period of 1½–2 hours the spontaneous motility was recorded for 2 hours on a smoked drum. Those strips which did not show any spontaneous motility during this period were tested by addition of 20 γ adrenaline to a bath volume of 20 ml.

Actomyosin. The determinations of myosin and actomyosin were carried out according to the viscosimetric method used by Naeslund, Snellman, Csapo and Erdös (1950).

Phase. The classification of the material was based on the case history correlated with a microscopical examination of the cyclic phase of the endometrium.

The patients were classified in four groups:

(1) *Proliferatory group:* containing patients with normal menstrual cycle and normal endometrium in the proliferatory phase.

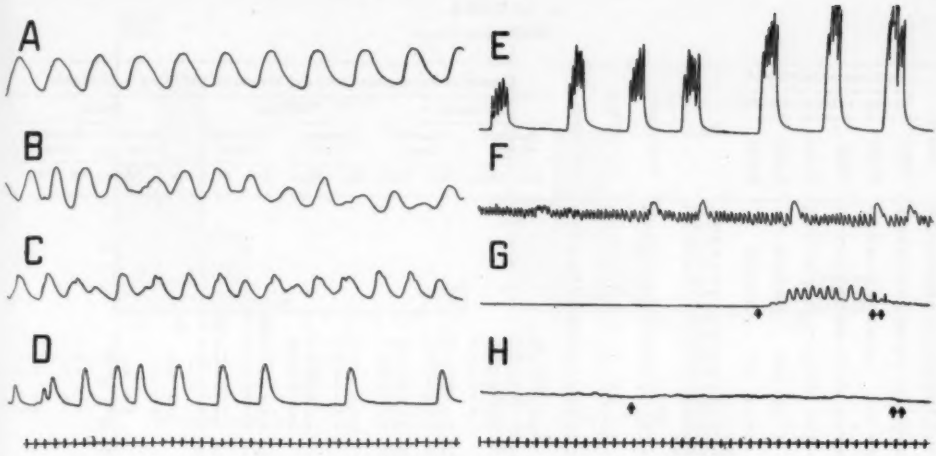

FIG. 1

Different types of motility distinguished.

A. Sinusoidal contractions.
B. Contractions similar to A but with varying base-line.
C. Contractions similar to A with varying amplitude but with constant baseline.
D. Single contractions with constant amplitude and baseline.
E. "Sphincter-like" contractions=contractions similar to D with small, rapid contractions superimposed.
F. Small, rapid contractions.
G. No spontaneous motility but response to adrenaline.
H. No spontaneous motility and no response to adrenaline.

(2) *Secretory group:* containing patients with normal menstrual cycle and normal endometrium in the secretory phase.

(3) *Pre-climacteric group:* containing patients with non-ovulatory bleedings or signs of insufficiency of the corpus luteum function.

(4) *Menopausal group:* containing patients who have not been menstruating for at least 4 years.

The material consisting of 84 cases is presented in detail in Tables I–V.

RESULTS

From a comparative study of the motility curves we were able to distinguish eight main types of motility pattern. During the period of recording each muscle strip showed a constant type of spontaneous motility.

The following patterns were distinguished (Fig. 1):

A. Sinusoidal contractions.
B. Contractions similar to A but with varying baseline.
C. Contractions similar to A with varying amplitude but with constant baseline.
D. Single contractions with constant amplitude and baseline.
E. "Sphincter-like" contractions=contractions similar to D with small, rapid contractions superimposed.
F. Small, rapid contractions.
G. No spontaneous motility but response to adrenaline.
H. No spontaneous motility and no response to adrenaline.

Definite types of motility were found to be rather characteristic of different parts of the uterus. However, no difference in the spontaneous motility could be demonstrated between the proliferatory and secretory phases of the sexual cycle.

In the corpus both of *the proliferatory and the secretory groups* (Tables I and II) the dominating types were A, B and C; D, E and F were characteristically absent (Fig. 2). In a few cases

TABLE I

Proliferatory Group

Case No.	Spontaneous Motility of Corpus Longit.	Corpus Transv.	Isthmus Longit.	Isthmus Transv.	Cervix Longit.	Cervix Transv.	Phase	Cycle (days)	Day of Cycle	Age (years)	Content of Actomyosin (Act.) and Myosin (Myo.) in mg./g. of Muscle: Corpus Internal Layer Act.	Corpus Internal Layer Myo.	Corpus External Layer Act.	Corpus External Layer Myo.	Isthmus Internal Layer Act.	Isthmus Internal Layer Myo.	Isthmus External Layer Act.	Isthmus External Layer Myo.	Cervix Internal Layer Act.	Cervix Internal Layer Myo.	Cervix External Layer Act.	Cervix External Layer Myo.
10	B	B	G	G			prolif.	28	9	42							8·4	11·9				
46	B	B	C	F			prolif.	28	10	50							10·3	11·7				
52	B	B	E	E			prolif.	28	11	41												
54	B	B	E	E	H	H	prolif.	28	11	50												
61	C	A	D	A	H	D	prolif.	30	5	40												
62	B	B	G	G	G	D	prolif.	28	8	48												
68	A	A	E	A	H	H	prolif.	28	11	31												
70	H	H	B	E	G	H	prolif.	28	13	46												
73	A	B	A	D	G	G	prolif.	25	6	42							8·4	11·9				
77	B	B	B	E			prolif.	28	11	46							10·3	11·7				
83	A	A	A	A			prolif.	28	8	40	12·6	14·2	22·2	15·3	3·7	9·2	4·2	8·2				
84	A	A	E	H	H	H	prolif.	28	8	39	3·8	17·1	5·2	11·3	5·0	11·5	11·3	11·3	0	7·8	4·1	7·4
85			C	C	H	D	prolif.	28	9	43	10·6	17·6	11·2	15·4	9·9	14·0	13·6	11·7	7·2	9·4	9·1	6·7
86	C		E	E			prolif.	28	11	38	11·1	14·3	18·2	19·6	7·5	13·6	13·4	13·9				
91	C	C	C		H	H	prolif.	25	10	45	15·9	13·5	14·4	14·2	8·7	10·6	9·5	12·3	3·4	9·1	4·4	8·9
93	C	C	H	A	H	G	prolif.	28–30	8	52	14·7	16·4	8·5	14·3	8·8	11·2	6·7	14·0	5·9	10·6	3·1	9·4
107	D		D	E		D	prolif.	24	5	48	12·2	12·2	14·0	10·0	2·6	8·5	4·6	7·8				
34	B	B	B	E	F	H	late prolif.	30	15	38												
71	B	B	B	E			late prolif.	28	?	53			15·2	12·9			8·3	9·5				
75	A	G	B	B			late prolif.	30	?	44	12·8	12·5	9·7	10·3			9·2	11·5				
78		B	A	C	F	F	late prolif.	28	?	47							4·1	7·6			3·0	5·3
82	B		B	B	H	G	late prolif.	28	19	43	10·8	13·9	10·8	14·2	5·8	9·6	6·4	11·0	2·4	6·3	3·4	6·8
87			G	E	H	G	late prolif.	27	12	43	10·1	13·6	14·8	14·3	3·7	10·1	7·1	10·2	3·1	7·0	4·1	8·6
95			E	E	G	G	late prolif.	28	10	50	24·2	22·1	15·6	13·9	4·3	10·9	6·7	9·9	0	8·6	3·6	8·5
104			H	B		F	late prolif.	26–27	10	47	17·1	15·1	19·9	15·5	3·8	9·7	7·6	8·9				
113	B		F	H	H	H	late prolif.	28	16	48	21·6	14·3	17·6	14·2	20·8	14·5	16·7	13·1				

TABLE II

Secretory Group

Case No.	Spontaneous Motility of Corpus Longit.	Corpus Transv.	Isthmus Longit.	Isthmus Transv.	Cervix Longit.	Cervix Transv.	Phase	Cycle (days)	Day of Cycle	Age (years)	Content of Actomyosin (Act.) and Myosin (Myo.) in mg./g. of Muscle: Corpus Internal Layer Act.	Corpus Internal Layer Myo.	Corpus External Layer Act.	Corpus External Layer Myo.	Isthmus Internal Layer Act.	Isthmus Internal Layer Myo.	Isthmus External Layer Act.	Isthmus External Layer Myo.	Cervix Internal Layer Act.	Cervix Internal Layer Myo.	Cervix External Layer Act.	Cervix External Layer Myo.
32	B	A	A	G	D	H	early secr.	25	?	36												
47	A	B	D	E	G	G	early secr.	?	18	40												
48	B	B	H	E	H	H	early secr.	21	12													
56	A	A	C	E	D	H	early secr.	27	16	43												
63	A	H	E	G	H	H	early secr.	28	9	54												
81	H	H	C	E			early secr.	28	14	39	11·0	15·3	13·6	15·3	9·5	12·6	11·8	12·6				
97	B	B	C	C	D	D	early secr.	28	17	44					13·0	14·0	3·6	8·0	2·6	5·5	2·4	5·6
100	B	C	B	B	H	H	early secr.	21	10	42	14·6	12·7	12·6	11·3	9·7	9·9	11·7	10·4	3·0	7·0	2·8	8·4
103	B		C	B			early secr.	28	16	44	16·0	13·7	13·7	15·4	11·5	13·0	8·8	12·1				
110	B		H	D		H	early secr.	28	21	46												
17	A		B				secr.	36	32	39												
18			E	E			secr.	28	26	40												
21	B	C	G	E			secr.	28	?	49												
22	A	A	G	E			secr.	28	28	47												
23	B		E				secr.	30	14	48												
24	C		E	G	H		secr.	26	26	45												
31	A	A	F	H			secr.	26	19	42												
35	A	A	B	E	H	H	secr.	?	25	51												
45			A	B			secr.	28	22	38												
60	A	C	D	G	D	G	secr.	26	?	49												
66	C	A	D	G	H	G	secr.	30	21	45												
72	C	B	G	G			secr.	28	23	50												
79	B	B	H	B	H	H	secr.	30	20	48			13·0	9·6			12·4	11·5			4·4	7·2
94	B	B	H	H	H	G	secr.	28	24	51	21·6	16·1	17·9	15·7			11·2	14·5	5·3	10·0	2·6	7·6
109	B	C	H	H	H	H	secr.	28	22	38												

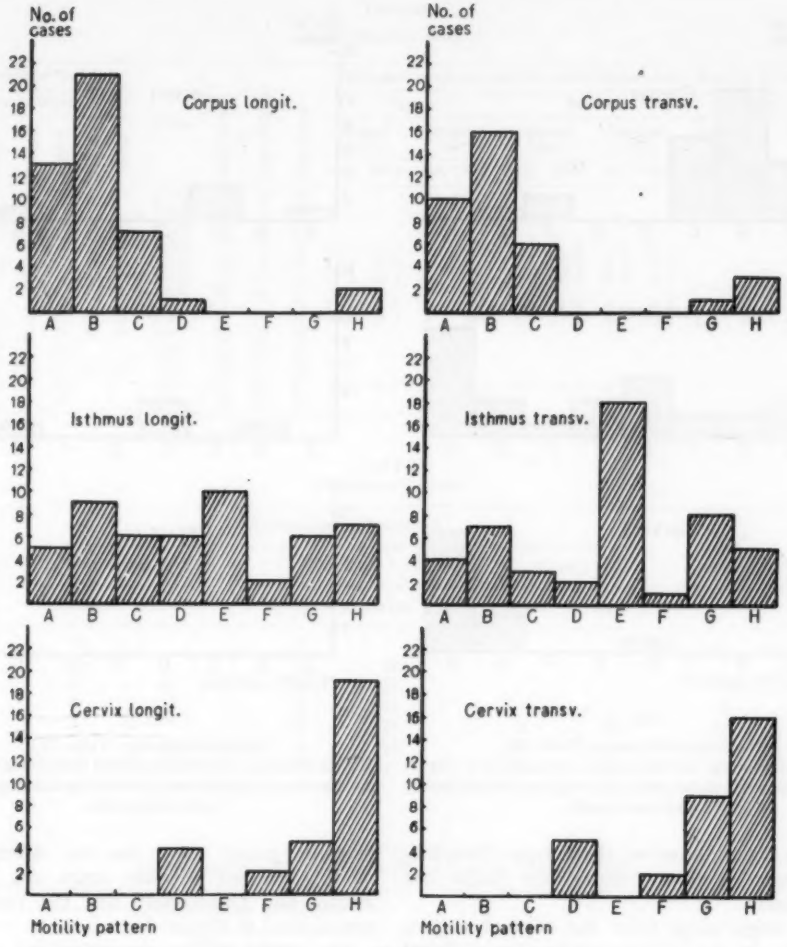

FIG. 2

Proliferatory and secretory groups (Tables I and II).

The distribution of motility pattern (according to Fig. 1) in different parts of the uterus. To the left muscle strips cut longitudinally and to the right cut transversely.

there was no spontaneous motility (Types G and H).

In the isthmus region all types of motility were represented, but the E motility dominated. This "sphincter-like" type of motility was not found in any other part of the uterus.

In the cervix the Types A, B, C and E were absent and in the majority of cases there was no spontaneous motility (Types G and H).

Between strips cut transversely and longitudinally no difference could be demonstrated either in the corpus or in the cervix. In the

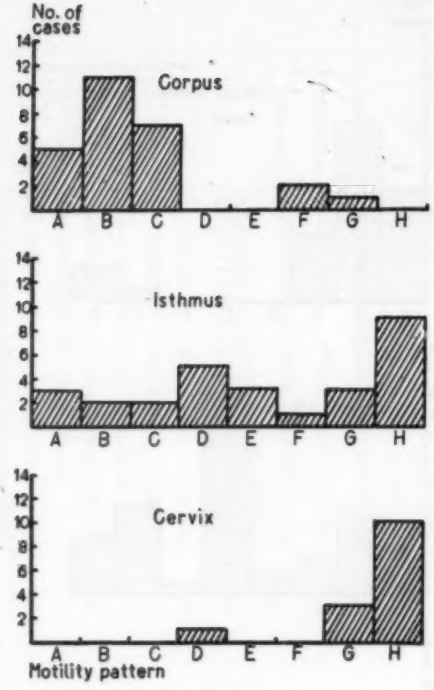

FIG. 3

Pre-climacteric group (Table III).
The distribution of motility pattern (according to Fig. 1) in different parts of the uterus for strips cut longitudinally and transversely.

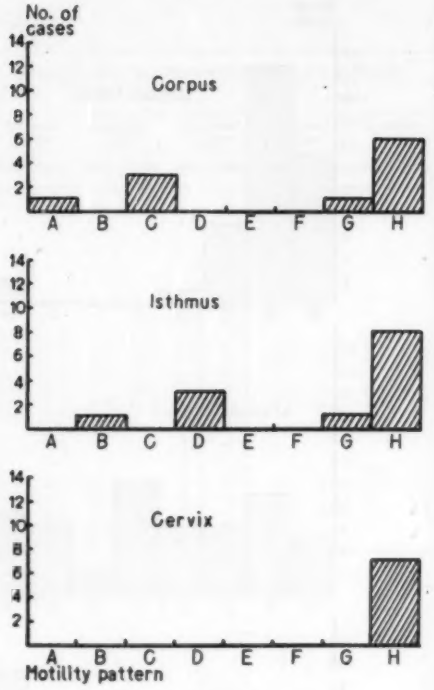

FIG. 4

Menopausal group (Table IV).
The distribution of motility pattern (according to Fig. 1) in different parts of the uterus for strips cut longitudinally and transversely.

isthmus region, however, the E type of motility was more common among the strips cut transversely.

The strips taken from the cornual regions showed only the spontaneous motility of Types A, B and C (see Table V).

In the *pre-climacteric group* (Table III) the same distribution of motility patterns was seen as for the uteri of fertile women. There was the same distribution of motility types in strips cut longitudinally and transversely. The results are summarized in Figure 3.

In the *menopausal group* (Table IV) only few cases showed spontaneous motility the oldest of which were 66 years with a menopausal period of 22 and 23 years, respectively. As in the previous group there was no difference in motility pattern between strips cut longitudinally and transversely and the results are summarized in Figure 4.

The results of the determinations of actomyosin and myosin are seen in Tables I–III.

In the corpus the actomyosin content of both external and internal layer was 14·2 mg./g. of muscle. In the isthmus region the corresponding figures were 9·0 for the external layer and 8·0 for the internal layer. In the external layer of the cervix the actomyosin content was 3·9 mg./g. of muscle and for the internal layer 3·3.

The myosin content of the external layer of the corpus was 13·7 mg./g. and in the internal layer 15·0 mg./g. For the isthmus region the

TABLE III

Pre-climacteric Group

Case No.	Spontaneous Motility of: Corpus Longit.	Corpus Transv.	Isthmus Longit.	Isthmus Transv.	Cervix Longit.	Cervix Transv.	Phase	Cycle (days)	Day of Cycle	Age (years)	Content of Actomyosin (Act.) and Myosin (Myo.) in mg./g. of Muscle: Corpus Internal Layer Act.	Corpus Internal Layer Myo.	Corpus External Layer Act.	Corpus External Layer Myo.	Isthmus Internal Layer Act.	Isthmus Internal Layer Myo.	Isthmus External Layer Act.	Isthmus External Layer Myo.	Cervix Internal Layer Act.	Cervix Internal Layer Myo.	Cervix External Layer Act.	Cervix External Layer Myo.
7	C		E				prolif.	28	27	46													
16	B	G		B			prolif.	28	?	47													
36	B	B	H	H	H	H	prolif.	30	?	42													
58	C	C		D	G	H	prolif.	28	20	45													
89			D	G	H	H	prolif.	?	?	50	12·1	11·2	8·1	12·3	9·5	11·4	10·0	12·8					
98	A	A	H	G	H	H	prolif.	28	8	54	11·5	13·4	9·8	11·3	3·4	7·6	4·7	7·1					
99	F	F	E	B			prolif.	28	25	53	17·0	10·7	13·1	10·7	10·0	10·1	10·0	8·4					
102	A		A	D			prolif.	29	20	47			11·4	11·1									
106	A		A	H			prolif.	?	?	53	11·9	12·3	10·1	7·0	2·5	5·9	3·6	7·5					
111	B	B	G	D	D	G	prolif.	21	3	40	14·7	15·2	14·3	12·3	6·2	15·4	8·9	10·6	4·3	8·3	4·5	9·6	
30	C	B	H	H	H	G	secr.	28	26	46													
43	B	B	F	C			secr.	25	24	42													
57	B	A	E	H			secr.	28	21	50													
67	B	C	A	D	H	H	secr.	25	21	46													
101	C	C	H	H			secr.	30	30	47	8·0	12·7	11·5	15·2	3·6	8·5	5·6	7·6					
108	B			C			secr.	28	23	42													

TABLE IV

Menopausal Group

Case No.	Spontaneous Motility of: Corpus Longit.	Corpus Transv.	Isthmus Longit.	Isthmus Transv.	Cervix Longit.	Cervix Transv.	Menopause (years)	Age (years)
4	H		H		H		11	56
6	H		H	H			7	60
25	C	C	H	H			4	52
42	H	H	H	H			6	55
64	A		B	G	H	H	22	66
65	G	H	D	H	H	H	13	61
90	C	H	D	D	H	H	23	66

TABLE V

Spontaneous Motility of Muscle Strips from the Uterine Cornua

Case No.	Spontaneous Motility of: Left Cornua Longit.	Left Cornua Transv.	Right Cornua Longit.	Right Cornua Tranvs.	Isthmus Longit.	Isthmus Transv.	Phase	Cycle (days)	Day of Cycle	Age (years)
114	H	H	C	C	H	H	prolif.	21	6	55
115	B	B	C	A	H	H	prolif.	28	11	42
117	G	A	A	G	H	H	prolif.	28	18	49
118	B	B	C	B		F	prolif.	28	34	48
119	B	B	B	A	D	H	prolif.	30	6	46
122	B	B	C	B			prolif.	30	22	41
123	C	B	C	C	E	E	secr.	28	28	41
125	B	B	A	A	D	E	secr.	?	?	43
126	A	B	B	A	A	A	secr.	28	35	47
128	B	A	A	A	H	H	prolif.	28	7	45

corresponding figures were 11·2 and 11·4 mg./g. respectively, and for the cervix the figures were 7·5 and 8·1 mg./g. respectively.

Thus, no difference was found in the content of actomyosin and myosin between the external layer and internal layer of the uterus, but the highest content of these substances was found in the corpus and the lowest in the cervix.

It was not possible to demonstrate any correlation between the type of motility and the content of actomyosin and myosin in any part of the uterus investigated.

Conclusions and Discussion

From the results obtained it is evident that the musculature from different parts of the uterus has a characteristic motility pattern. It is, however, not possible to demonstrate a correlation between the type of motility and the content of actomyosin and myosin.

Like Naeslund *et al.* (1950) we have found the highest content of actomyosin and myosin in the corpus and the lowest in the cervix.

During the different sexual phases no differences in the types of motility could be demonstrated. We have not performed a quantitative study of the amplitude of the contractions because such an investigation requires the same constant isotonic registration in all cases. Del Sol Fernandez (1951) stated that the amplitude of the contractions varied with the sexual phases, but his description of the experimental conditions does not permit such a conclusion.

The motility in the menopausal group is very scanty and the pre-climacteric group shows an intermediate distribution of motility types.

The motility pattern of Type E found in the isthmus region may be the functional explanation of the sphincter effect of the internal os described by Westman (1942).

We have found this pattern both in strips cut longitudinally and transversely. This observation is explained by the fact that the muscle fibres in this region have a spiral-like arrangement according to Goerttler (1930).

This type of motility seems to be confined to the isthmus musculature *per se*. We were not able to demonstrate any influence of the sexual phase. This fact is, however, not contradictory to the observations *in vivo*, by Asplund (1952) and Borell and Fernström (1953) which showed a contraction of the internal os during the secretory phase, because our muscle strips were studied in an organ-bath, without any influence of hormones or innervation.

Muscle strips from the uterine cornua were studied in order to see if a similar motility could be demonstrated in this region, since the internal opening of the tube may act as a functional sphincter. However, no such sphincter-like motility could be demonstrated either in the strips cut longitudinally or in the strips cut transversely.

We have also studied the influence of drugs on these motility patterns, and the results obtained will be described in Part II of this paper.

Summary

Muscle strips have been cut longitudinally and transversely from different parts of 84 non-pregnant uteri and studied qualitatively *in vitro* using the Magnus-Kehrer technique. Eight main types of motility were found (Fig. 1). The distribution of motility types was characteristic for the various parts of the uterus (Figs. 2–4). In the corpus sinusoidal contractions were most common. In the isthmus single contractions with or without a "sphincter-like" pattern superimposed were prominent. And in the cervix the spontaneous motility was poor. The "sphincter-like" contractions were only found in the isthmus.

The content of actomyosin and myosin was highest in the corpus and lowest in the cervix and no difference between the outer and inner layer could be demonstrated. No correlation was found between the content of the contractile proteins and the type of motility.

We are indebted to Statens Medicinska forskningsråd and Styrelsen för Kungl. Farmaceutiska Institutet (Anslaget för främjande av medicinsk forskning vid institutet) for financial support of this investigation.

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INVERSION OF THE BLADDER AS A COMPLICATION OF LARGE VESICO-VAGINAL FISTULAE

BY

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A REMARKABLE complication of a vesico-vaginal fistula of large size is an eversion of the bladder through the fistula. In its lesser degrees a protrusion is not uncommon, and it presents as a soft, red, velvety mass plugging the fistula or pushing its way through the fistula into the vagina. It is of course the *anterior* bladder wall which first everts, and in most cases the process is limited to that wall. In extreme cases however the whole organ turns inside out (inverts) and fills the vagina, or even bulges far beyond the vulva. In a series of more than 175 cases of vesico-vaginal fistula (Moir, 1954, 1956) referred to the Nuffield Department of Obstetrics and Gynaecology for treatment, there have been some 8 or 10 instances of pronounced bladder eversion, and 2 of complete inversion.

With the patient in the lithotomy position and the perineum depressed by a Sims's speculum, the protruding bladder with its exposed mucosal surface can be clearly seen; and the tumour can be made to increase still more in size by asking the patient to strain. When, however, the patient is placed in the knee-chest position the local appearance is conspicuously changed. Because of gravity the everted bladder is now withdrawn; air rushes in, and both the vagina and bladder become widely distended making the anatomical limits of the fistula much more clearly defined (Fig. 1). This was, of course, the finding that so impressed J. Marion Sims more than 100 years ago, and which induced him to attempt the operative cure of vesico-vaginal fistulae; the influence that Sims's work was to have on the subsequent development of gynaecology is well known (Moir, 1940).

When a vesico-vaginal fistula is associated with bladder inversion it usually follows that the ureters are situated at or close to the vaginal edge. The exact position of the orifices must be clearly identified before operative treatment is undertaken. In some cases the tell-tale spurts of urine, rhythmically ejected, make identification easy; in others it is only by careful search with the probe that the orifices can be found.

The pressure from the inverted bladder, if long sustained, may cause one or both ureters to become grossly dilated. In the second of the cases to be described this change was so great that a medium-sized rubber catheter, passed into the bladder by way of a preliminary investigation, disappeared entirely from sight and touch; only after a long search was the mystery solved by finding that the catheter had passed into a grossly dilated ureter, where it occupied a position far behind and to the side of the bladder. In this connexion, the importance of a preliminary intravenous pyelography examination to detect any possible ureteric or kidney abnormality is obvious.

CASE 1

Mrs. E.C., age 50

For 27 years Mrs. E C., who lived in a remote part of Wales, had suffered from complete incontinence of urine; the trouble dated from a difficult forceps delivery.

Two years after the original injury an operation for the repair of a vesico-vaginal fistula had been attempted but was unsuccessful. Believing herself to be incurable this unfortunate woman had resigned herself to a life of constant wetness. Some measure of her affliction may be gathered from a simple calculation which showed that she must have washed and dried, during this period, not less than 68,875 pieces of Turkish towelling

and used countless hundreds of packages of cotton wool to sop up the incessant welling of urine.

In spite of her disability this woman had two further pregnancies. During the second of these she became aware of "something falling down"; this something was diagnosed by the district nurse to be a falling of the womb. In recent years the condition had become more and more troublesome and had eventually forced her to seek further advice from a nearby medical centre. There it was found that the prolapse was no falling of the womb but a protrusion of the bladder itself. Through the kindness of the Medical Officer, Mr. Gareth Jones, the patient was sent to the Nuffield Department of Obstetrics and Gynaecology at Oxford.

Examination revealed a large, soft, fleshy mass projecting far beyond the vulva. It was a completely inverted bladder (Fig. 2). The surface was clean, and pinkish-white in colour. A small portion removed for biopsy showed the surface layer to consist of a modified squamous epithelium. There was no keratinization, but the general appearance was more akin to normal skin than to bladder mucosa (Fig. 3).

The inverted mass was easily replaced, and when pushed back revealed the large defect in the anterior vaginal wall through which it customarily protruded; this was a vesico-vaginal fistula measuring rather more than one inch in diameter, situated at and just above what at one time must have been the vesico-urethral junction. Both ureteric orifices could be seen just within the margins of the fistula where they periodically ejected fine streams of urine. The uterus and cervix were normal in size and position, although the cervix could be easily drawn downwards with a volsella (Fig. 4).

Operative repair was surprisingly easy. The vaginal wall was incised for one-third of an inch beyond the "north" and the "south" margins of the fistula, and these incisions were then joined at a deep level round the edges of the fistula. After a little freeing and undercutting, the vaginal edge was excised with scissors to give a broad, slanting, surface leading down to the bladder mucosa. The inner layers (the submucosal structures of the bladder) were joined with an inrolling, continuous catgut suture (B.P.C. No. 3/0 size), followed by a shorter second row of catgut stitches to build up the muscle in the region of the bladder neck. The main union—the approximation of the trimmed vaginal walls—was brought about in the usual way with a series of No. 5 monofilament nylon sutures inserted as deep, mattress stitches to bring about a broad approximation of the prepared vaginal edges (Fig. 4). The bladder was drained by means of a catheter stitched to the lip of the meatus, and the drainage helped by gentle suction from hydrostatic bottles. The drainage was discontinued on the 14th day, and the nylon sutures were removed on the 21st day.

It is remarkable to record that the bladder function quickly returned to normal. Four weeks after the fistula operation a pelvic floor repair was performed. The patient left hospital in excellent condition on the 38th day after the original operation and has since remained well.

A cystoscopic examination undertaken before the patient's discharge showed a healthy bladder wall without any signs of cystitis. A minute biopsy specimen of bladder mucosa was again obtained; it did not show any material change from the earlier sample.

Case 2

Mrs. M.S., age 58

This patient, a rather feeble woman of low mentality, had previously had an abdomino-perineal resection of the rectum and part of the anterior vaginal wall; this was done for a granulomatous tumour which was said to be vaginal rather than rectal in origin.

In the 21 years since this operation the patient had been in poor health and had suffered from anaemia; at one time the haemoglobin level was as low as 38 per cent. For considerably more than 10 years she had suffered from complete incontinence of urine, and for several years there had been a feeling of "something coming down". The patient was referred for treatment by Mr. H. Burton of Stoke-on-Trent to whom my thanks are due.

Examination showed a soft, fleshy, globular mass at the vulva. It was almost as large as a billiard ball, and the surface was extensively ulcerated (Fig. 5). The tumour was a completely

inverted bladder which, when pushed back, revealed a vesico-vaginal fistula described by her own doctor as "tremendous in size". The fistula involved most of the trigone of the bladder and nearly the whole of the urethra; only a bridge of tissue remained, and that was situated over the external urinary meatus. Both ureteric orifices could be seen at the edges of the fistula. One of them (the left) was grossly dilated; and during the subsequent operation the blades of a closed pair of scissors could be easily slipped inside its cavity. Intravenous pyelography was attempted, but for technical reasons was not entirely satisfactory although both kidneys were seen to be functioning reasonably well.

As in the previous case, the operative repair was less difficult than anticipated. The small remaining portion of urethra was completely divided and the edges retracted to show the full extent of what had once been the urethra. Although the urethral gutter was now exposed it was difficult to identify the margins, for the transformed mucosa merged imperceptibly with the epithelium of the vaginal wall.

A thin polythene tube was laid in position and stitched to the remains of the external urinary meatus; it acted both as a splint on which to rebuild the urethra and, later, as a catheter for drainage of the bladder. Parallel incisions, about 1·5 cm. apart, were made down both sides over the supposed positions of the old urethral edges, and these incisions were merged with the upper edge of the fistula and extended over the bladder neck. After a little undercutting, a running stitch of fine catgut was used to unite the inner edges of the fistula (as in Case 1) and to create, by inward folding, a new urethra over the catheter. The bladder neck was tightened by two separate catgut stitches (No. 0 B.P.C. size). The main part of the repair—namely, the broad apposition of the vaginal wall from both sides over the whole extent of the fistula and reconstructed urethra—was accomplished by a series of 10 interrupted nylon sutures inserted as vertical mattress stitches. The subsequent bladder drainage was aided by gentle suction and was maintained for 14 days. The nylon stitches were removed on the 21st day.

For some weeks this patient could void urine only with difficulty; and twice daily catheterizing showed a residual urine volume that varied from 6 to 10 ounces. Gradually, however, the residual urine lessened, and after 6 weeks normal bladder function became established. Cystoscopy performed previous to the patient's discharge showed a normal bladder mucosa. Indigo carmine injected intravenously appeared at the right ureteric orifice in the normal manner; but on the left side there was some delay, and the dye escaped as a slow wave, or cloud, rather than as the normal jet. The urine from both ureters was clear and not obviously infected.

Comment

The extreme degree to which the bladder may invert through a vesico-vaginal fistula is well shown in the two recorded cases. Despite the extensive nature of the original injury, the long exposure of the bladder to external traumata, and the period of time during which the bladder muscular action had been in abeyance (27 years in the one case and more than 10 years in the other), normal function was quickly restored after the local repair.

While the cases presented are extreme examples of bladder protrusion, lesser degrees of the same condition, such as the case depicted in Figure 1, are not unusual. In a series of 175 cases of vesico-vaginal fistula (mostly complicated or intractable cases referred from other centres), there have been some 8 or 10 in which a remarkable bulging of the anterior bladder wall through the fistula was seen; in many more the condition was present in a minor form but was not specially recorded in the notes.

The operative treatment of these cases is not necessarily difficult. Indeed, the prospect of cure may be better than it is in the case of a smaller fistula caused by radium damage, or one associated with gross distortion of the vesico-urethral junction after, for example, a Millin sling operation—types of case which have, in my experience, caused much greater trouble.

The possibility of direct operative cure should be emphasized, for I have known of cases in which the surgeon, confronted by an inversion of the bladder, has needlessly transplanted the ureters into the colon and excised the inverted organ.

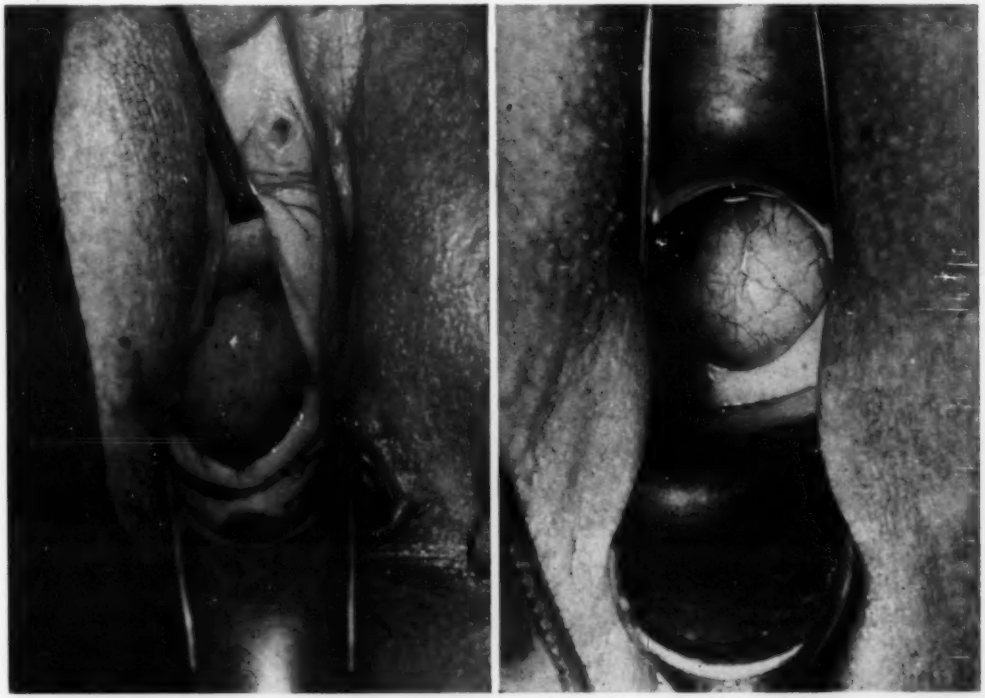

FIG. 1

A large vesico-vaginal fistula showing bladder protrusion.

Left: The appearance with the patient in the lithotomy position; the anterior bladder wall is bulging through the fistula.

Right: The appearance with the patient in the knee-chest position; the bladder is now withdrawn and is ballooned out with air. The network of blood vessels in the bladder mucosa is clearly seen.

FIG. 2

Colour photograph showing bladder inversion (Case 1). (The skin has been painted with proflavine antiseptic which has given it a yellow tint.)

FIG. 3
Photomicrograph of the bladder mucosa (Case 1).

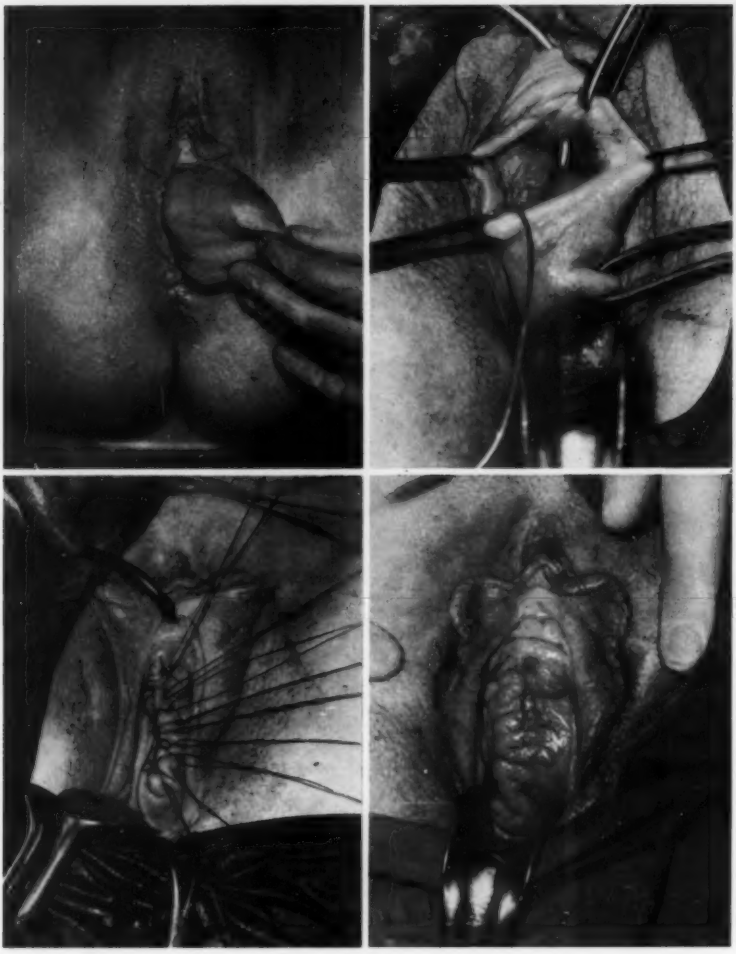

FIG. 4

Inversion of the bladder (Case 1).

Top left: Condition before operation (compare with Fig. 2).

Top right: The bladder has been pushed back and the fistula exposed. There is a bladder-sound in the urethra, and a probe in the right ureter. The cervix has been drawn down to show its position relative to the fistula.

Bottom left: The completion of the operation. The "mattress" nylon sutures have been tied but are not yet cut. A catheter is tied to a stitch which anchors it to the lip of the external urinary meatus.

Bottom right: The condition three weeks later after removal of the nylon stitches.

J.C.M.

FIG. 5
Inversion of the bladder (Case 2).

ACKNOWLEDGMENTS

Case 1 has already been very briefly reported in the *Proc. R. Soc. Med.* (1953, **46**, 844) and an illustration has appeared in the *Lancet* (op. cit.). Half of Figure 1 and a part of Figure 4 have appeared in *Amer. J. Obstet. Gynec.* (op. cit.). I am grateful to the publishers, the C. V. Mosby Company, for permission to use these pictures again. The photomicrograph was kindly supplied by Dr. H. Cowdell of the Radcliffe Infirmary Pathology Department.

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SUTURE OF THE CERVIX FOR INEVITABLE MISCARRIAGE

BY

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LITTLE is known of the aetiology of miscarriages which occur during the middle three months of pregnancy. My interest in sphincteric incompetence of the cervix as a possible aetiological factor was provoked by the following case:

Case 1. Mrs. M., aged 35, was seen at the North Middlesex Hospital in August, 1951. Her first pregnancy, 10 years before, had terminated in a difficult forceps delivery. The child, which weighed 8 pounds 3 ounces, died from cerebral injury after 3 days. Subsequently she had 4 miscarriages, each one at 24 weeks of gestation. In 1950 a fibromyoma, 4 inches in diameter, was removed surgically from the fundus of the uterus.

She became pregnant 12 months later; her expected date of delivery was May, 1952. The patient was admitted to hospital on 3rd February, 1952, complaining of low backache and a mucous discharge. Examination revealed a uterus enlarged to the size of 24-weeks gestation. The cervix was sufficiently dilated to admit two fingers and the membranes were bulging through the internal os. A purse-string suture of No. 2 chromic catgut was placed around the cervix.

On 28th February examination revealed dilatation of the cervix had recurred and another purse-string suture was inserted. This was twice repeated at fortnightly intervals. On 18th April, when speculum examination revealed cervical dilatation, no suture was inserted and within 2 hours, after a few strong contractions, she was delivered normally of a male child weighing 6 pounds 4 ounces.

This case, the first that I know to be successfully treated by ligation of the cervix during pregnancy, led me to look for instances in which the loss of the normal sphincteric control allowed herniation of the contents of the uterus and their subsequent expulsion.

INVESTIGATION

This report deals with a series of 70 cases on whom ligation of the cervix was performed for inevitable miscarriage. All cases presented with dilatation of the cervix and bulging of the forewaters during the second trimester and all, with one exception, had one or more previous miscarriages. These previous miscarriages occurred at approximately the same time in succeeding pregnancies and usually they commenced with rupture of the membranes followed by a short and relatively painless labour.

Most cases presented between 20 and 24 weeks of gestation (Fig. 1). It was at this stage that ligation was most effective and no success has been achieved before the 20th week. The average duration of pregnancy at the time of ligation in successful cases was 22 weeks and, in failed cases, 19 weeks (Fig. 2). Assuming that ligation succeeds only in cases of mechanical weakness,

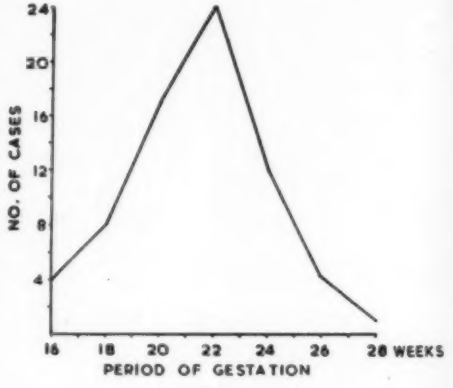

FIG. 1

Graph showing the period of gestation when ligation was performed in 70 cases.

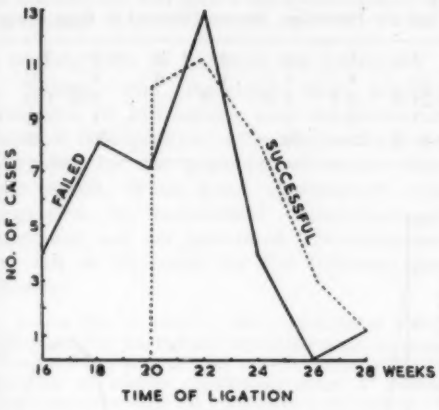

FIG. 2

Graph showing the period of gestation when ligation was performed successfully and unsuccessfully.

the inference is that this predisposes to miscarriage only after the fourth month of pregnancy. Non-mechanical factors may bring about termination of pregnancy at any time.

The relevant past history of the patients (Table I) shows an abnormally high incidence of

TABLE I

Previous Operations on the Cervix of Patients Presenting With Late Miscarriages

Operation	No. of Cases	Percentage
Dilatation and curettage ..	30	42·9
Dilatation for dysmenorrhoea ..	5	7·1
Amputation of cervix	3	4·3
Cauterization of cervix ..	15	21·4
Trachelorrhaphy	1	1·4

operative dilatation of the cervix. Dilatation and curettage is a common procedure and in many cases may have followed a miscarriage, in which circumstance one would not anticipate cervical damage. On the firm nulliparous cervix the trauma may be severe and permanent. The five patients in this series who had a dilatation for dysmenorrhoea had suffered a tragic procession of miscarriages. Between them, in 18 pregnancies, only one living child was produced and this died from prematurity. In 4 of these 5 women a successful outcome of pregnancy followed ligation of the cervix. The following case illustrates a serious sequel to too-forceful surgical dilatation:

Case 2. Mrs. L., aged 30, had received treatment in a mental ward for depression. The psychiatrist related this to the 6 miscarriages, each at about 20-weeks gestation, which had occurred during the previous 5 years. Surgical dilatation of the cervix had been performed at the age of 17 to treat severe dysmenorrhoea.

She was first seen on 6th April, 1955, because termination of her seventh pregnancy on psychiatric grounds had been proposed. The estimated date of delivery was 15th November, 1955. It was decided to allow the pregnancy to continue and to examine the cervix at weekly intervals.

On 1st June, when the patient presented with a profuse discharge, speculum examination revealed the membranes protruding through the internal os which was relaxed to admit 2 fingers.

A purse-string suture of silk was inserted. Subsequent regular examinations showed the cervix to remain closed.

On 20th September, the patient was admitted with bearing down pains and backache. The stitch had pulled out and the bag of forewaters was protruding into the vagina. Within an hour she was delivered of a premature male infant weighing 3 pounds 8 ounces. This child has since flourished and there has been an amazing change in the mental attitude of the patient.

Many patients had been treated by cauterization of the cervix. This is a common procedure in parous women and its high incidence may be of no importance. It is suspected that the number of cauterizations may indicate an abnormally high proportion of cases of cervical trauma within the series and it is that which leads to incompetence. There was no relation between the degree of success with ligation and the previous use of the cautery, in fact of the 15 patients there was a successful result in only 3.

In the Manchester repair operation there is a danger of removing the cervix above the level of the internal os and 3 such cases were seen with total amputation of the cervix and resulting incompetence.

The following case illustrates a possible sequel to excision of the cervical sphincter:

Case 3. Mrs. R., aged 45, had a Manchester repair performed 2 years after the breech birth at term of an infant in 1936. The infant lived only 3 days. Since then she has been pregnant at least 9 times. Each pregnancy terminated shortly after the membranes ruptured at about 5 months.

The patient was seen in our unit on 4th July, 1955, when

TABLE II

The Number of Consecutive Miscarriages Prior to Ligation and the Percentage Success Obtained in Each Group

No. of miscarriages	0	1	2	3	4	5	6	7	8	9	Total
No. of cases	1	4	16	24	17	4	2	1	0	1	70
Percentage	1·4	5·7	22·9	34·3	24·3	5·7	2·9	1·4	–	1·4	100
No. of successes	1	3	6	13	7	1	1	–	–	1	33
Percentage success	100	75	37·5	54·2	41·2	25	50	–	–	100	43

she was 20-weeks pregnant. Speculum examination showed the membranes were bulging but the cervix had been amputated flush with the vaginal vault. It was therefore impossible to insert the usual purse-string ligature. A deep mattress suture of silk was placed through the lower pole of the uterus and complete closure obtained.

The pregnancy continued until 10th November, 1955, when lower abdominal pains and backache signified the onset of labour. A lower segment Caesarean section was performed because of the successful repair of the prolapse and a living child weighing 4 pounds 9 ounces was delivered.

Of all factors pre-disposing to incompetence, child-birth appeared to be the most important. In this series 43 patients had carried to term prior to the appearance of cervical incompetence. All except one suffered from a varying number of miscarriages before ligation (Table II).

Table II shows that a successful outcome following ligation is not related to the number of previous miscarriages. When a normal birth had occurred subsequent to miscarriage the operation was not performed.

Some cases have no apparent history of trauma. These may have a congenital laxity of the cervix but this is speculative. One patient who had a bicornuate uterus was found to have a single cervical canal which was lax in both the pregnant and non-pregnant states. Cervical ligation succeeded in 2 pregnancies.

Of the 70 patients in whom ligation was performed, 33 gave birth to infants who survived. Sixteen others had their pregnancy extended by periods exceeding 4 weeks but the offspring did not survive. In Figure 3, which shows the duration of pregnancy following ligation, it will be seen that when the method fails it does so most frequently in the first week. Those cases in which the suture holds for more than 5 weeks are usually successful. The majority deliver themselves prematurely, the average period of gestation being 35 weeks in the successful cases.

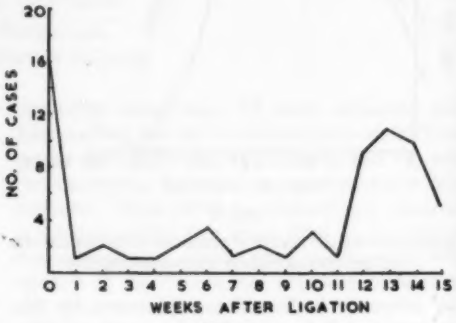

FIG. 3

Graph showing the duration of pregnancy after ligation of the cervix of 70 patients.

DIAGNOSIS OF CERVICAL INCOMPETENCE

Patients who suffer from cervical incompetence in pregnancy may present with the following symptoms:

(1) *Vaginal Discharge.* This is prominent and arises from the discharge of the operculum as the cervix dilates. Examination for suspected moniliasis has often led to the discovery that the discharge is in fact the operculum and bulging membranes have been seen.

(2) *Lower Abdominal Discomfort.* If this is suspected to be of uterine origin during the middle trimester the cervix should be examined.

(3) *A Lump in the Vagina.* On 3 occasions this has proved to be the bag of membranes protruding beyond the external os.

Speculum examination of the cervix is now performed at weekly intervals on all patients with a previous history of repeated miscarriages in the second trimester and most cases are

diagnosed this way before the appearance of any symptoms.

Selection of Patients for Ligation

Patients who presented with bleeding, toxaemia or hydramnios were considered unsuitable for operation. Intra-uterine death was excluded by the presence of recent foetal movements. When foetal abnormalities were suggested by radiological examination the operation was not performed. The importance of this is illustrated by the following case history:

Case 4. Mrs. G., aged 25, had a miscarriage at 8-weeks gestation. This was followed by dilatation and curettage. Two years later she presented at 24-weeks gestation complaining of uterine contractions every 5 minutes. Examination revealed the membranes to be bulging well into the vagina through a cervix which would admit 3 fingers. Under ether anaesthesia, a purse-string suture of braided silk was placed around the cervix and tied after the hernial protrusion of the membranes had been reduced. Strong contractions continued, necessitating division of the stitch 2 hours later. Within minutes the patient delivered herself of an anencephalic foetus.

It has become apparent that patients in strong labour with the intact membranes bulging beyond the external os are generally not suitable. It is too late. Ligation is contra-indicated also if the membranes are ruptured. As selection of cases has improved, so have our results; in the first 35, 13 cases were successful, in the second 35, 20 cases.

Operative Technique

The anaesthetic has usually been nitrous oxide together with intravenous Flaxedil following induction by sodium thiopentone. The patient is placed in the lithotomy position and the vulva and vagina prepared, care being taken not to rupture the membranes. The bladder having been emptied, the cervix is exposed and grasped at each quadrant by Allis' or Babcock's forceps (Fig. 4). If necessary the bulging bag of membranes is reduced by one or two dampened swabs held on sponge forceps. A broken capsule of amyl nitrite placed under the anaesthetic mask has been tried as a means of reducing tension. Its advantage is doubtful.

A purse-string suture of No. 4 Mersilk on a Mayo needle is inserted around the exo-cervix as high as possible to approximate to the level of the internal os. This is at the junction of the rugose vagina and smooth cervix (Fig. 5). Five or six bites with the needle are made, with special attention to the stitches behind the cervix. These are difficult to insert and must be deep. If the ligature pulls out later, it is always from this portion, the silk remaining attached to the anterior lip. The stitch is pulled tight enough to close the internal os, the knot being made in front of the cervix and the ends left long enough to facilitate subsequent division (Fig. 6).

No trouble has been caused through ischaemia of the cervix; it is sufficiently vascular at this time to provide adequate blood-flow between the bites of the suture.

After-Care

After operation the patients are kept in bed for 3 to 7 days. Painful contractions may occur for 24 hours following the stimulation of the uterus and for this morphine sulphate is administered but the ligature is not divided. Should labour become established the ligature will pull out from the posterior lip. As no harm has followed this, it is better to allow it to happen than to lose hope of success. The cervix is inspected on the next day and a bacteriological report obtained on a high vaginal swab. Infection has not been a significant problem.

Subsequently the patient returns weekly for examination and she is warned to report any symptoms. It has been necessary on 6 occasions to repeat the operation because the original suture has cut out. Three of these were ligated with catgut. Of the remainder, only one had a successful outcome. This suggested that factors other than incompetence were operating.

The silk stitch is divided and removed when labour becomes established or at the 38th week of pregnancy. A short labour follows usually and delivery is effected with ease. All cases except 2, who had Caesarean sections for obstetrical reasons, were delivered normally.

Discussion

It may be argued, as no controls have been possible, that the pregnancies at the time of suture would have continued despite ligation. I believe, in view of their previous histories, the patients themselves acted as controls.

Case 5. Mrs. C., aged 25, aborted her first pregnancy at 3 months in 1949. Dilatation and curettage were performed. In 1950 and again in 1951 she miscarried during the fifth month of pregnancy.

On each occasion rupture of the membranes had preceded a short labour.

She was seen by me on 16th December, 1954, in the 22nd week of her fourth pregnancy when she complained of lower abdominal pains and a vaginal discharge. The cervix was found to be dilated to admit 2 fingers and the membranes protruded to the level of the external os. Cervical ligation was performed.

The pregnancy continued and the silk was divided at 35 weeks. She did not come into labour until another 2 weeks when after a few contractions she was delivered of a normal child of 7 pounds 2 ounces.

In 1956 the patient again conceived when under the care of another doctor. It was thought this time the cervix was firmer and nothing was done. She aborted completely at the 22nd week of pregnancy.

At this stage it is not possible to account for success in some patients and failure in others. It appears that in some the forewaters protrude under considerable tension (Fig. 7), while in others there is little tension (Fig. 8). This was not realized at the beginning of the series and thus the records do not discriminate between the two groups. It is my impression that success follows ligation of the non-tension group. In the tension group there is probably some factor responsible for irreversible stimulation of the uterine muscle. Urinary pregnanediol estimations are now being performed on cases to be ligated and it is hoped that these may lead us closer to the nature of this factor.

Other sources of failure are related to faulty technique. The stitch must be high enough and tight enough to prevent future herniation of the membranes. Silk is not the ideal suture material. It is inelastic and does not take up with the cervix and so may pull out. An improved material is now being sought.

Accidental perforation of the membranes sometimes occurs during operation. This is understandable because the amnion, which usually herniates through the ruptured chorion presents a very thin membrane. I have on several occasions tied a small perforation with catgut and one of these carried to term uneventfully.

As the series has progressed it has become clear that factors other than mechanical operate to produce incompetence of the cervix on some occasions. Whatever these factors prove to be, we know that certain women previously denied children can now be offered some hope with the help of cervical ligation.

Summary

(1) Miscarriages which occur in the middle trimester of pregnancy are sometimes due to incompetence of the cervical sphincter.

(2) Regular speculum examination of patients who have had repeated miscarriages has revealed on many occasions dilatation of the cervix.

(3) The modes of clinical presentation of cervical incompetence are discussed.

(4) Treatment by ligation of the cervix in selected cases with a silk suture during pregnancy is detailed.

(5) Results from 70 cases so treated are analyzed and recorded.

Acknowledgments

The compilation of a series of cases dealing with a rare condition such as this depended upon the co-operation of many of my colleagues of the Footscray Hospital and of the Royal Women's Hospital, Melbourne. It would be unfair to discriminate but exceptions must be made of Doctor Donald F. Lawson and Doctor Frank M. C. Forster through whose interest and stimulus this paper largely came to be written. To all these people I extend my grateful thanks. Thanks are also due to Miss M. L. Johnson who prepared photographs.

FIG. 4

Bulging membranes displayed through a dilating os. The cervix is grasped at each quadrant with Babcock's forceps.

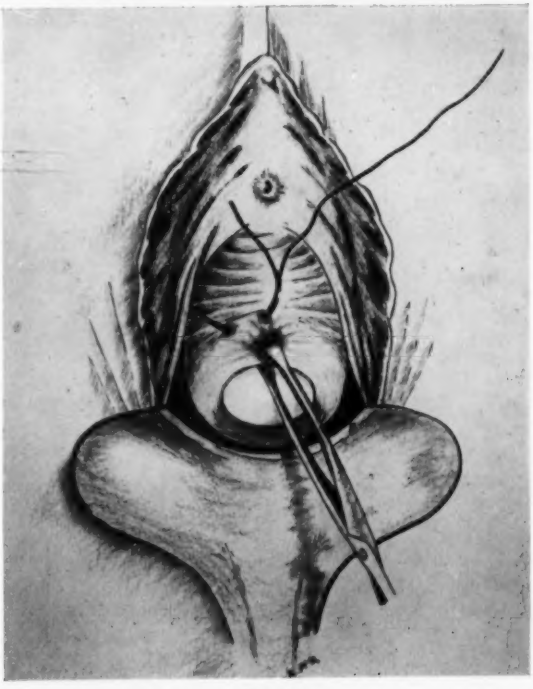

FIG. 5

The purse-string suture is inserted at the junction of cervix and vagina to approximate to the level of the internal os.

FIG. 6

The appearance of the cervix after the ligature has been tied.

FIG. 7

The bag of membranes bulging with considerable tension through the cervix.

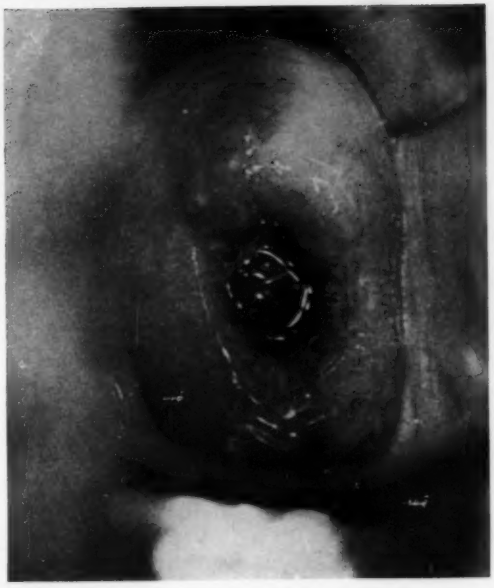

FIG. 8

The forewaters appear at the cervix but without tension.

METHODS FOR IMPROVING THE RESULTS OF FORCEPS DELIVERY*

Including An Improved Obstetric Forceps

BY

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IT is generally agreed that the teaching and general use of obstetric forceps has greatly improved over the past 50 years. Standard textbooks fairly well outline the indications and contra-indications for their use, both on behalf of mother and child. Possibly the weakest point in the teaching of forceps delivery is a failure to grasp a few of the fundamental mechanical principles involved. Hospital facilities, anaesthetics, antibiotics, etc., have developed greatly, but very little has taken place in the development or improvement of the instrument itself.

As this thesis presents an instrument incorporating some fundamental mechanical principles not previously employed, it would only be fair to analyze some of the previous instruments and methods and suggest where they might be improved. The introduction of a new method or instrument can only be justified if it is an improvement on what has gone before.

There are several good instruments in general use today, and some have been designed for the management of certain abnormal vertex presentations. Generally speaking, these instruments are modifications of Smellie's. The instrument in current use which most closely resembles Smellie's is the Simpson and it is available with or without an axis-traction device.

The blades are fenestrated and possess a double curvature. The first or cephalic curve is obviously designed to give an accurate cephalic application. The extremities of the blades fit on either side and under the chin, not behind the chin as so frequently and incorrectly illustrated in current textbooks.

The real reason for the second curve is not so obvious. The radius of this second curve is at right angles to that of the first and it has unfortunately become known as the "pelvic curve". Actually, it is just as much a *cephalic* curve as the first. Smellie and Levret introduced this curve quite independently of each other and Smellie referred to it as "the second curve"—a much better name than pelvic curve for the following reason. The shape of a baby's head while in the maternal pelvis is neither spherical nor ovoid, but it is an ovoid with the long dimension curved in the direction of the mento-occipital axis. When straight blades—that is, without the so-called pelvic curve—were applied to a head in mid-pelvis, in the occipito-anterior position, the application was unsatisfactory. The shanks of the instrument being elevated by the perineum caused the tips of the blades to lie over the face. It is obvious that traction applied in this position would increase extension of the head and it often caused the blades to slip off completely, with consequent severe laceration to the birth canal, so the second curve was actually introduced to correct this deficiency. A proper definition of this second curve would be; it is that curve which is required to carry the long axis of the blade from a point just anterior to the posterior fontanel to curve gently forward and end in the chin. This is the most efficient line of application of blades for any forceps manœuvre, either rotation or traction. With a well designed instrument it is in most cases not too difficult to obtain. It so happened that in the case of heads in an occipito-anterior position this second curve fell in the direction of the pelvic axis; as a result it has been incorrectly named.

* Received the prize awarded in the Autumn of 1956 by the Council of the Royal College of Obstetricians and Gynaecologists for the best essay on this subject.

This instrument was originally designed for traction. Certain modifications of it have been used in the construction of instruments more suitably designed for rotation. The earlier forceps used either the French or English type of lock but more recent instruments, designed to facilitate application where asynclitism is present, use locks especially designed for the mechanical principle involved. The earlier instruments being chiefly designed for applying traction were not too well suited for the job of rotating.

Some authors are still inclined to give Tarnier credit for introducing the principle of axis-traction. There are numerous records of satisfactory instruments and methods for correct application of traction before Tarnier's time. Although Tarnier's forceps is a good instrument it is unnecessarily cumbersome and clumsy. It has many unnecessary parts and too many joints and swivels. The flexibility in the traction tackle of this instrument seems to appeal to its admirers, but many of these same enthusiasts, in teaching the use of the instrument, emphasize the importance of maintaining the traction rods in a fixed relation—parallel—to the shanks or handles. An extremely elementary knowledge of fundamental mechanics will show that the minute one movable part of a traction system is held in a fixed relation to another part, the function of the joint connecting these members is at once removed, and the device in effect becomes a rigid instrument. To provide a completely satisfactory axis-traction instrument, it is only necessary to bend the handle down so that the traction force may be applied to the instrument at a point which will allow it to be carried through the perineum and extend into the long axis of the blades (Fig. 1). It is just as easy to apply a traction force in the wrong direction with the many traction devices that have been suggested, as it is to apply it in the correct direction with a simple instrument of the above design.

The common mistake is that of applying traction so that the head is pulled forward toward the symphysis. To correct this it is only necessary for the obstetrician to grasp the traction handle with one hand and insert the index finger of the free hand between the symphysis and the advancing occiput. Undue pressure on the finger simply means that the line of traction should be lowered. It must be remembered that the flexibility of the operator's wrist, elbow, and his position, are all part of the traction system and they are entirely adequate. The traction rods in Tarnier's instrument are not only unnecessary, but their very presence produces a needless encroachment on an overtaxed perineum.

Special Methods for Dealing with Abnormal Vertex Presentations

It has long been recognized that one of the commonest deviations from the normal in vertex presentations is the occipito-posterior position arrested in the mid-pelvis. A large percentage of posterior positions rotate and deliver spontaneously. We are here concerned with those which do not behave so favourably.

If forceps delivery is indicated when the head is arrested in the mid-pelvis with the occiput posteriorly it is commonly conceded that correction of the malposition is indicated before any attempt at extraction by forceps is to be considered. Manual rotation of the head, in spite of all the suggested technics, simply consists of what the term applies—grasping the head with the hand and rotating it into an anterior position. This, of course, is done under anaesthesia, and in a good many cases is accomplished with ease. Whether or not it is the method approved by present-day obstetricians, it should still be taught to the beginner before he attempts what might be considered as more intricate manœuvres.

Forceps Rotation

In some cases, where the head has become deeply engaged, manual rotation becomes extremely difficult and sometimes impossible. Fully 100 years before Scanzoni described his method, Smellie gave a detailed account of using the forceps as a rotator. After an unsuccessful attempt at manual rotation Smellie described the application of the forceps to the head in the position in which it presented. By gently pushing up on the head he rotated it into the corrected position. As Smellie (1754) preferred his straight forceps—without the "second

curve"—for this manœuvre, it was not necessary to remove and re-apply them. Scanzoni used a forceps with a pelvic curve, and so they had to be removed and re-applied to the corrected position following rotation. Some forceps are more suitable than others for this manœuvre and Bill (1925) has given an excellent account of his method using the Tucker-McLane forceps.

The Transverse Arrest

This position may result from a posterior position arrested in rotation or it may be due to a head that originally engaged in the transverse diameter and became arrested in descent due to the malposition. Just as in occipito-posterior positions some of these latter presentations rotate and deliver spontaneously. When they become arrested the management is essentially the same as for occipito-posterior positions. In 1915 Kielland presented a forceps especially designed for the management of these particular cases. Although there were earlier forceps with a sliding lock to accommodate for asynclitism, Kielland's was the most satisfactory. The objection to this instrument is that the blades spread too much at the tip. The blades are crossed as in the conventional forceps, and so do not remain parallel to each other.

Pre-requisites of a Good Obstetric Forceps

(1) The blades should be well designed to give an accurate cephalic application.

(2) A sliding lock is essential to accommodate for asynclitism.

(3) The blades should face parallel to each other at all times, and be readily adjustable to variation in head size.

(4) The instrument should be simple of construction, and mechanically simple to use (Fig. 2).

The Author's Forceps

Another forceps has been designed by the writer which is not to be confused with the one incorporating the universal joint produced some years ago. This first instrument was well suited for the rotation and delivery of occipito-posterior positions, but its scope was limited in that it was difficult to apply to transverse positions where there was marked asynclitism. The new instrument has abandoned the universal joint at the junction of the blades to the shank. It relies for its flexibility on a special type of sliding lock which accommodates for asynclitism, and also for the changing presenting diameter as asynclitism is corrected. Nearly all the forceps in current use consist essentially of two members which cross at the lock. This, from the point of view of desirable traction is a distinct disadvantage because the larger the head the more the blades have to spread, and as the spread—due to the obvious leverage—is twice as great at the tips of the blades as it is at the biparietal diameter, the forceps slide up the face as traction is applied. The larger the head the more the blades have to spread, and it is in these cases where the greatest amount of traction is generally required. The new instrument has a special lock which is split in two; each half may slide up and down on the corresponding shank. The shanks do not cross and throughout any adjustment to variation in head size the blades face parallel to each other at all times. When applied to a head in asynclitism either blade may be in advance of the other, depending on the type—anterior or posterior—or degree of asynclitism. The instrument automatically adjusts itself as the asynclitism disappears during rotation. In spite of its ready adaptability the instrument is extremely simple in construction and operation (Figs. 3 (*b*), 4 (*b*)).

Application of the Forceps

(1) *To Transverse Positions*

The anterior blade is first applied. It is inserted up the hollow of the sacrum and made to sweep around either the occiput or face until it comes to lie on the anterior aspect of the head. The posterior blade is inserted just as with the Kielland. The lock is then fastened permitting for any asynclitism (Fig. 5). A word description of the locking device is unnecessarily cumbersome and a moment's inspection of the instrument makes the arrangement obvious at once. The traction handle is purposely designed as part of the lock so that rotation or traction cannot be applied until it is securely in place. The further advantage of this attachment is that

when traction is applied *no compression of the handles*, with resulting compression of the head, can occur.

Most operators will agree that one of the greatest difficulties in securing a proper application to a head in the transverse position is obstruction from the perineum. In difficult cases, regardless of the type of instrument used, an adequate episiotomy should be done *before* attempting application of the instrument. In many cases this makes the difference between a difficult application and a relatively easy one, and there is no better way of protecting the perineum from the certain amount of unavoidable manipulative trauma. In these difficult cases it is essential to get the blades directed well up into the pelvis. This can only be done if the shanks of the instrument are well depressed (Smellie). This in turn can only be accomplished if the perineal obstruction is removed as much as possible. The objection that early episiotomy produces too much bleeding before the head can be brought down to control it is not valid. It is only necessary to pick up the bleeding points with artery forceps as in any other surgical procedure. When a satisfactory application has been obtained the instrument is locked on the head.

When forceps are applied to a head in a transverse position, the blades obviously cannot be described as right and left. They become anterior and posterior; and the "so-called" pelvic curve is not in line with the pelvic axis at all. Hence the author's objection to the term. As mentioned above, this curve is still required to obtain application of the blade to the proper line of application on the head. This cannot be secured with a straight blade. In cases with deep impaction, rotation is facilitated by pushing gently up on the forceps during rotation. In cases with some degree of flat pelvis, it is sometimes advisable to apply traction with the head in the transverse position, and gently rotate as the head approaches the outlet. Traction is then continued to complete delivery without re-application of the forceps (Fig. 1).

(2) *To Posterior Positions*

The instrument is simply turned upside down and the blades are applied exactly as if the head were in the anterior position. When the blades have been placed in satisfactory position, the traction handle is applied in the reversed position so that it will be ready for traction when rotation is completed (Fig. 6). Here again, the so-called pelvic curve is reversed, but the blade is directed into the pelvis by the angle at which it leaves the shank. When rotation is accomplished, traction is applied to complete delivery without re-application of the instrument.

(3) *To Anterior Positions*

The instrument is just as adaptable to anterior positions as any standard instrument and the simple mechanics of the traction device are illustrated in Figure 1.

In conclusion, it should be stated that in the field of manipulative obstetrics countless other methods and instruments have been devised from time to time. It would not be possible or advisable to attempt to include them all in this paper. Suffice it to say that some methods are more applicable in certain situations than others. In evaluating the various methods and instruments, it is well to remember that it is not so much the method or instrument but the man using it that counts. Whether one approves of the various manipulative procedures that have been taught does not matter, but the more one knows about other people's methods, the more efficiently and intelligently is he able to apply his own.

This instrument has not been previously published anywhere. It has been used with eminent satisfaction by several of my colleagues and myself for over three years. As no modifications are considered necessary, it is now in the process of manufacture for distribution to the profession.

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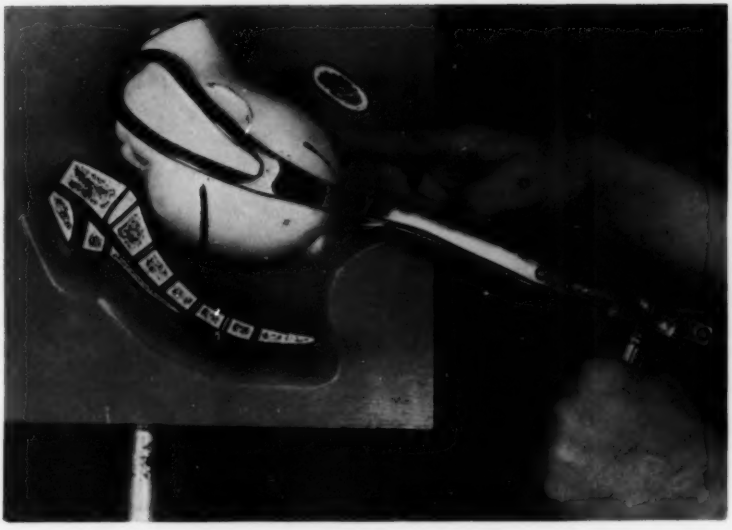

FIG. 1

Shows an accurate application of blades to the head in an occipito-anterior position. Traction is applied by the grip on the handle provided. The index finger of the free hand indicates the *direction* of traction in the proper axis of the pelvis.

FIG. 2

This instrument seems to fulfil the requirements here mentioned.

FIG. 3

(*a*) A conventional forceps adjusted to minimal head size.

(*b*) The improved forceps adjusted to minimal head size.

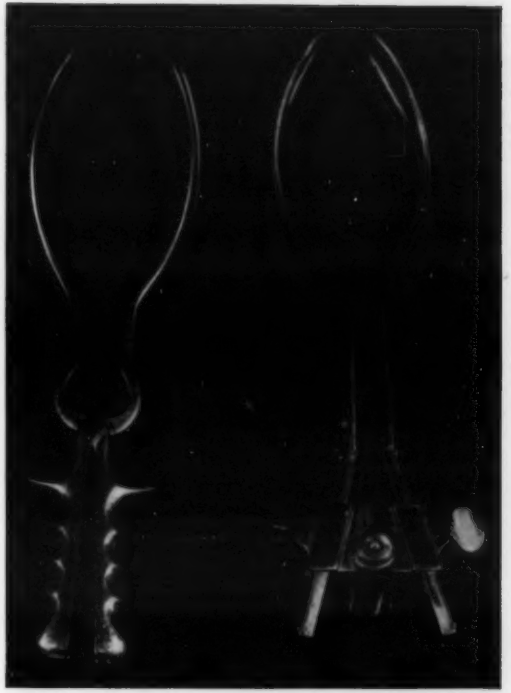

FIG. 4

(*a*) A conventional forceps adjusted to increase in head size. Note spread of blade tips, decreasing efficiency of traction grip. *Crossed shanks and blades.*

(*b*) The improved forceps adjusted to same increase in head size. Note no spread at blade tips, maintaining efficiency of traction grip. *Parallel shanks and blades.*

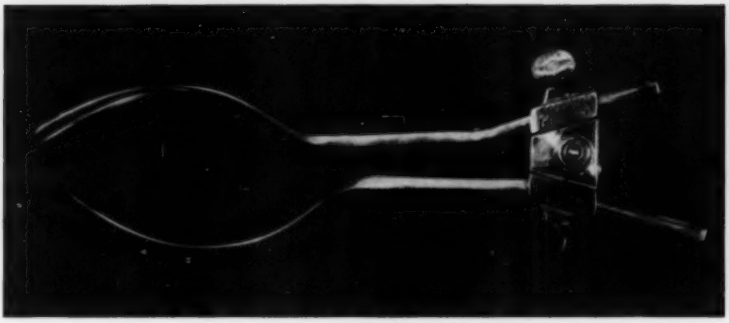

FIG. 5

The sliding lock provides adjustment to asynclitism. Regardless of head size the blades are always parallel to each other.

FIG. 6

Application of the forceps to an occipito-posterior position. Following rotation, delivery is completed as in Figure 1, without re-application of the instrument.

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UTERINE PROLAPSE AND PROLAPSE OF THE VAGINAL VAULT TREATED BY SACRAL HYSTEROPEXY

BY

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IT is our intention to describe a new operative procedure for extensive uterine prolapse, or prolapse of the vaginal vault or enterocele, but before doing so it is perhaps desirable to define some of the terms commonly used and to discuss the aetiology of these forms of genital prolapse.

ANATOMICAL CONSIDERATIONS

In the first degree of uterine prolapse, the cervix descends below its normal level but does not project outside the vulva; because of its descent the uterus tends to retrovert but it is not necessarily retroflexed. In second degree uterine prolapse the cervix protrudes outside the vulva on straining. In third degree prolapse, also known as procidentia, the whole uterus is outside the vulva on straining. However, it may be difficult to define the uterine fundus accurately, and a more exact description of third degree prolapse is uterine descent with complete eversion of the anterior vaginal wall; the posterior vaginal wall may or may not be completely everted. The term "procidentia" only means a falling down, or prolapse, and is sometimes used for both second and third degrees of uterine prolapse; that is, all cases in which the cervix projects outside the vulva. A strict distinction between the second and third degree of prolapse is perhaps unnecessary, the degree varying with the intensity of straining, and is maximal when traction is applied to the cervix under anaesthesia. In many cases of third degree prolapse the prolapse remains outside without straining, the vaginal walls becoming thickened and oedematous and sometimes ulcerated.

Many patients suffering from uterine prolapse, particularly if they are parous women, have some degree of cystocele or rectocele or both, but these forms of genital prolapse may occur with little or no uterine prolapse. It must be made clear that whenever there is any uterine descent the bladder inevitably descends with the uterus, because of its close attachment to the anterior vaginal wall and supra-vaginal cervix. Marked bulging of the anterior vaginal wall on straining, after replacement of the cervix to its normal position with a volsellum forceps, indicates a true cystocele as distinct from the pseudo-cystocele which inevitably accompanies uterine prolapse. A rectocele may also accompany uterine prolapse, but does not necessarily do so, and the posterior vaginal wall may be considerably or completely everted by uterine prolapse without any rectocele. Replacement of the cervix to its normal position in patients with third degree uterine prolapse may leave some laxity of the posterior vaginal wall without any rectocele.

It must also be noted that in all cases of uterine prolapse the peritoneum of the pouch of Douglas is invariably stretched and elongated because of its attachment to the posterior aspect of the supra-vaginal cervix and to the upper part of the posterior vaginal wall. This is a potential enterocele; the size of this peritoneal pouch varies considerably and in some patients the pouch contains coils of bowel or omentum. The term "Pouch of Douglas hernia" is often used instead of enterocele, particularly when this type of prolapse occurs without uterine prolapse.

The term "vault prolapse" may be used to describe uterine prolapse, but it must be recognized that the vaginal vault may prolapse after a hysterectomy, abdominal or vaginal, total or sub-total. It is perhaps surprising that vault prolapse does not occur more often after hysterectomy and that it should be more common after a sub-total than a total hysterectomy; it must be concluded that the vault prolapse in such cases is due to a pre-existing tendency to prolapse rather than to the operation of hysterectomy. Furthermore, there can be no doubt that uterine prolapse cannot be cured simply by removal of the uterus and indeed, the ensuing vault prolapse is more difficult to cure once the uterus has been removed. Sometimes an enterocele appears as a sequel to the Manchester operation for repair of a uterine prolapse and it may also follow the Mayo operation (1915) in which the uterus is removed *per vaginam* and the broad ligaments sutured together to support the abdominal contents. Gray Ward (1936) maintained that an enterocele occurred in 18·2 per cent of Mayo operations and that, even after his modification for obliteration of the peritoneal cul-de-sac and suture of the utero-sacral ligaments, it still occurred in 10 per cent of cases.

It is well known that in some cases of second degree and third degree uterine prolapse the length of the uterine cavity is sometimes increased and may measure 4 or 5 inches. Malpas (1955) states that it often measures 7 or 8 inches but, in our series of 45 patients having abdominal section for extensive uterine prolapse, no such extreme enlargement was seen. The uterus may sometimes be long and thin and it is generally believed that this is due to elongation of the supra-vaginal cervix resulting from the prolapse of the uterus. Malpas (1955) makes a distinction between a general prolapse, with considerable peritoneal herniation but without any elongation of the cervix, and utero-vaginal prolapse in which there is elongation of the supra-vaginal cervix, with little enterocele. We find it impossible to accept the validity of this distinction and do not believe that the tough inelastic supra-vaginal cervix can possibly be stretched by uterine prolapse when there is no kind of fixation of the body of the uterus. Even when the body of the uterus has been fixed by ventrofixation, there may be no increase in the length of the cervix at all, yet the uterus may again prolapse with a fibromuscular band still attaching it to the anterior abdominal wall. The probable explanation of the increase in length of the uterine cavity when it does occur, and it is by no means common, is that a large bulky uterus has undergone post-menopausal atrophy and prolapsed at the same time. Finally, it must be appreciated that the fascial structures supporting the uterus must have undergone stretching to the extent of 3 or 4 inches in second degree prolapse, and 6 or 7 inches in third degree prolapse. No one would claim that the shortening of Mackenrodt's ligaments achieved by the Manchester operation is of such an extent; the success of this operation depends largely on the re-building of the levator diaphragm on which the cervix normally rests and on narrowing of the vaginal introitus.

Aetiology of Uterine Prolapse

The uterus is kept in its normal position in the pelvis by its fascial supports, namely, the cardinal ligaments of Mackenrodt and the utero-sacral ligaments. Unlike most ligaments these fibromuscular condensations of the pelvic fascia tend to fan out and become lost before they reach the side walls of the pelvis and sacrum, and for this reason doubt has arisen as to their functional importance. Nevertheless, most gynaecological surgeons are in no doubt as to their importance in maintaining the uterus and other pelvic organs in their normal positions.

The uterus tends to descend on straining or coughing and, under these circumstances, the muscular pelvic diaphragm formed by the levator ani muscles lends additional support to the pelvic viscera.

Uterine prolapse is essentially due to weakness of its fascial supports. This may be inherent or congenital weakness in multiparous as well as in nulliparous patients with prolapse, but is more obviously due to the atrophic changes which accompany the menopause. Uterine prolapse may occur, though not invariably, when the muscular pelvic diaphragm is weak and when the vaginal introitus has been enlarged by tearing of the perineal body, so that the cervix

lies directly over the introitus instead of being supported at times of stress by the levator diaphragm.

Berglas and Rubin (1953) have made extensive studies of the supporting structures of the uterus, both by histological examination of the pelvic connective tissue and by X-ray myography, and they have concluded that there is no anatomical basis for assuming that the pelvic organs are supported by the connective tissue structures. They maintain that the levator diaphragm is solely responsible for the support of the pelvic viscera and that uterine prolapse is essentially due to a defective muscular pelvic diaphragm, due to birth injury or some other structural or functional impairment. It is necessary to refute this with the following observations:

(1) A patient may show marked deficiency of the levator muscular diaphragm and a complete perineal tear, present perhaps for many years, with no uterine prolapse at all.

(2) Third degree prolapse may be seen in a nulliparous patient with an undamaged and normally functioning pelvic diaphragm. It has sometimes been suggested that there is some inherent weakness of the levator muscles in nulliparous, and perhaps in some parous women with prolapse, because of an association with spina bifida occulta. However, Gemmell and Whitaker (1948) have pointed out that the definition of spina bifida occulta is often imprecise; they concluded that there was no relation between the occurrence of spina bifida occulta and uterine prolapse.

(3) The levator ani muscles can be fully relaxed by anaesthesia, but even so the cervix cannot normally be pulled down to or beyond the vaginal introitus without division of the supporting ligaments, as in the operation of vaginal hysterectomy.

(4) Repair of the muscular pelvic diaphragm by posterior colpo-perineorrhaphy does not necessarily prevent, nor will it cure, extensive uterine prolapse.

It is not to be wondered at that the fascial structures supporting the pelvic viscera should sometimes fail in their task, because of the assumption of the upright posture and the additional strain on these supports in a patient with chronic cough or constipation and advancing years; this is almost enough to account for most cases of uterine prolapse. It is indisputable that far more cases of uterine prolapse are seen in parous than in nulliparous women. Of course most women over forty have borne children, but it must be agreed that parturition increases the risk of prolapse, particularly in working women. Cystocele and rectocele may be due to an over-large foetus stretching the vaginal walls and underlying fascia; but uterine prolapse cannot be explained in this way and may follow the birth of quite a small child. Bearing down efforts before full dilatation of the cervix may weaken the fascial supports, and it is probable that the supporting structures are sometimes strained by forcible attempts at expulsion of the placenta before it has separated from the uterus; in such circumstances the congested cervix may be seen protruding from the vulva. Lawson and Lister (1954) reported that procidentia is common amongst Nigerians in Ibadan owing to the universal belief that when the membranes rupture voluntary expulsive efforts should begin; if the cervix does not happen to be fully dilated, it descends in front of the foetal head. Other cases originated in efforts to deliver the retained placenta by the patient or her relatives.

The Surgery of Uterine or Vault Prolapse

Early gynaecological surgeons relied on amputation of the cervix, combined with a posterior colpo-perineorrhaphy for the cure of the uterine prolapse, a technique practised by Donald in Manchester and Olshausen in Berlin from about 1886, when anaesthesia and Listerian methods of antisepsis were established. Kelly (1886) and Olshausen (1886) also advocated ventrofixation to the abdominal wall in patients with extensive uterine prolapse after the menopause. Fixation of the uterus to the anterior abdominal wall has rightly become obsolete as a method of curing uterine prolapse, chiefly because it allows the full force of the intra-abdominal pressure to fall on the poorly supported peritoneum of the pouch of Douglas; enterocele is a more or less inevitable sequel, and in many cases the uterus again prolapses,

although still adherent to the abdominal wall by a long fibromuscular band.

Fothergill (1908) modified Donald's operation by making a triangular incision in the anterior vaginal wall to allow exposure and suture of the parametric tissues, which he believed were important in holding up the uterus. This operation, described by Fletcher Shaw (1933) as the Manchester operation has held pride of place for half a century in the treatment of uterine prolapse. It provides an opportunity for repair of a cystocele or rectocele, as well as curing many cases of uterine prolapse, even though the operation inevitably leaves a laxity of the uterine supports, concealed, as a rule, by a well-performed perineorrhaphy. Donald (1921) stressed the importance of building up a firm posterior wall by deep buried sutures in the levator ani muscles. Nevertheless, the Manchester operation is not entirely satisfactory for extensive prolapse of the uterus because of the extreme stretching of the supporting ligaments, and it is followed by an enterocele or a recurrence of uterine prolapse in a number of cases.

Removal of the uterus by the Mayo or Gray Ward technique has not satisfactorily overcome this defect and many surgeons believe that an abdominal approach should be reconsidered for the surgical cure of extensive uterine prolapse after the menopause. Schubert (1914) used strips of fascia from the linea alba or external oblique to stitch the cervix up to the anterior abdominal wall. Grant-Ward (1938) used preserved ox fascia to suspend the vaginal vault after total hysterectomy, and Brady (1936) anchored the vaginal vault to the anterior abdominal wall with braided silk sutures. Suspension of the cervix or vaginal vault by strips of external oblique aponeurosis, carried behind the peritoneum on either side of the rectus abdominis muscles, was described by one of us (Arthure, 1949) to avoid the unnatural forward displacement of ventro-fixation, and at the same time obliteration of the pouch of Douglas was attempted by approximation of the utero-sacral ligaments or a Moschowitz suture (1912). The cavernous nature of the pouch of Douglas in many of these patients with procidentia often made this difficult.

It was then suggested by one of us (Savage, 1951) that the difficulty could best be overcome by fixation of the fundus of the uterus in the region of the sacral promontory. This leaves the cervix slightly higher than its normal position, with the vaginal canal directed upwards and backwards in its normal axis; access to the enlarged pouch of Douglas can be almost completely cut off by peritoneal suture (Fig. 1). A preliminary anterior colporrhaphy may be necessary if a large true cystocele is present, but laxity of the posterior vaginal wall or a markedly deficient perineal body can be ignored unless there is a big rectocele. Sjövall (1946) described a posterior interposition operation in which the body of the uterus was used to occlude a large utero-sacral hiatus, but we believe that skeletal fixation of the uterus is more likely to be permanent.

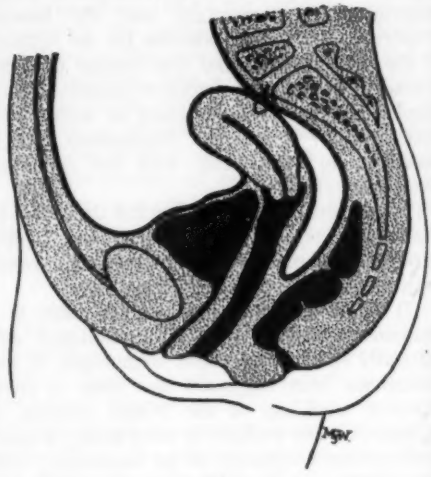

FIG. 1

Fixation of the uterus to the sacral promontory, showing obliteration of the pouch of Douglas.

OPERATIVE TECHNIQUE

The abdomen is opened by a median subumbilical incision, with the patient anaesthetized and in the Trendelenburg position. When the uterus is pulled upwards in a patient with a third degree prolapse it will be observed that it comes much farther than in a patient with undamaged

fascial supports; the pouch of Douglas is large and deep, and the utero-sacral peritoneal folds tenuous or absent. Coils of intestine are pushed upwards with abdominal packs, and the posterior parietal peritoneum over the sacral promontory is picked up and divided longitudinally with scissors, the incision extending for four or five inches. This incision is made to the right of the pelvic mesocolon and the right ureter should be identified and avoided. The fatty areolar tissue is then carefully dissected to define the right common iliac artery down to its bifurcation and the underlying common iliac vein. There is considerable variation in the relation of these vessels to the sacral promontory, but there is usually no difficulty in exposing the right side of the promontory and the ala of the sacrum, from which arises the anterior ligament of the sacro-iliac joint. The iliac vessels may be displaced a little outwards with a retractor before the fixation sutures are inserted. Two silk sutures are passed with a trocar-pointed cervix needle through the ligamentous tissue or through the superficial part of the intervertebral disc between the 5th lumbar vertebra and the sacrum (Fig. 2). It is advised that the surgeon should stand on the left side of the patient and pass the needle from without inwards to avoid the possibility of injury to the common iliac vein. The two stitches are then used to approximate the posterior aspect of the fundus or uterine body wherever it comes to lie spontaneously, without tension, in relation to the sacral promontory. Suture of the cervical stump or vaginal vault after hysterectomy may be possible, but every effort must be made to avoid undue tension. The divided posterior parietal peritoneum is now sutured with fine catgut to the right round ligament, starting on the side wall of the pelvis and coming inwards to the fundus of the uterus and to the left round ligament in its inner part; the outer two-thirds of the left round ligament is lightly stitched to the peritoneal coat of the pelvic colon (Fig. 3). In this way access to the pouch of Douglas is only possible on the outer side of the pelvic mesocolon by an opening which it is hoped will not permit herniation of small bowel. After removing the abdominal pack the abdomen is closed.

It has been found that this short and simple operation is well tolerated by elderly women, even though they may have an ulcerated procidentia. Post-operative complications are few compared with vaginal plastic operations. This operation of sacral hysteropexy, as we have called it, is recommended only for women after the menopause suffering from extensive uterine or vault prolapse or a large enterocele. A preliminary curetting may be advisable to exclude endometrial pathology in some cases, and an anterior colporrhaphy should always be done first if there is any true cystocele. Sacral hysteropexy does not prevent or make painful subsequent intercourse, which is sometimes found after the Manchester or Gray-Ward operation and, of course, after a Le Fort operation.

Follow-up Report

Since 1951 the operation has been performed 50 times in women whose ages ranged from 44 to 79 and 12 patients were over 70. All except one were past the menopause. Only 2 have not been traced and there have been no deaths in the remaining 48 patients. The follow-up interval has not been very long, of course, in some cases. In 45 patients the indication for operation was marked uterine descent, which was complete or third degree in 34 cases; in 7 of these the cervix or vaginal wall was badly ulcerated; only 3 were nulliparous. In addition the operation was performed on 4 patients with very large enteroceles protruding from the vulva; on one occasion the operation was performed for a large rectal prolapse with only moderate uterine descent.

Eleven patients had undergone a previous vaginal repair operation, and one other patient had had a ventro-fixation. Four patients had previously had a sub-total and one a total hysterectomy.

It was originally intended that the abdominal operation should be performed alone in the majority of cases in order that the efficiency of the fixation procedure should be tested without any vaginal repair. Only 2 patients had a perineal repair performed at the same time, and one of these had a small recto-vaginal fistula. It was, however, soon realized that, whilst sacral hysteropexy might cure uterine prolapse and enterocele, an increased strain is thrown

on the bladder and anterior vaginal wall after this operation whenever there is an increase in intra-abdominal pressure. Anterior colporrhaphy was therefore performed before stitching up the uterus on 13 occasions when there was a considerable cystocele, but even so there were 2 recurrences of cystocele, insufficient to cause symptoms; in addition 10 other patients have developed some degree of cystocele since the operation. These recurrent cystoceles have not given rise to any discomfort comparable with that of the uterine prolapse and one has been completely controlled by a plastic ring pessary. For the purpose of this review they have not been counted as failures, as the primary condition of uterine prolapse has been satisfactorily cured. Only 4 rectoceles have been noted in the follow-up examination and all have been symptomless.

In the series of 43 cases of extensive uterine prolapse attending for follow-up there have been 2 complete failures with recurrence of uterine prolapse and one partial failure in that the enterocele was not completely controlled; one other patient who did not attend for examination reported that she still had some prolapse. In addition there was 1 partial failure in the group of 4 large enteroceles, as a small enterocele persisted. The patient who had a large rectal prolapse has been completely cured, with no anal incontinence, which is particularly noteworthy in view of the fact that this condition is notoriously difficult to cure. Muir (1955) stated that 60 per cent recurred after rectosigmoidectomy and over half the cured patients were left with some incontinence.

Altogether there have been 5 failures in the 48 patients who have been followed up, but it must be recognized that the series is made up of cases of extensive prolapse, many of which would be regarded as difficult to cure by vaginal plastic procedures.

This report on the results of 5 years' experience of this operation of sacral hysteropexy leaves us satisfied that it has a place in the surgical treatment of severe degrees of uterine or vault prolapse and enterocele. We believe that these results will be further improved by greater experience of the operation and by preliminary anterior and posterior colpo-perineorrhaphy in some cases. When hysterectomy has already been performed, it is probable that the operation of vault suspension, previously described by one of us (Arthure, 1949), is preferable.

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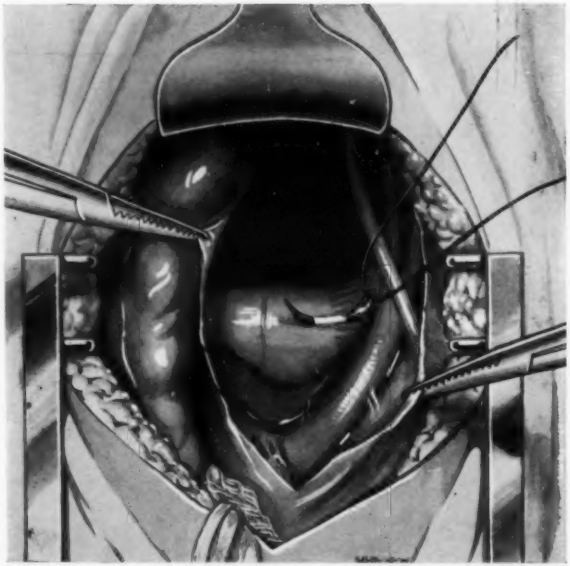

FIG. 2

Showing the posterior retro-peritoneal dissection, with a fixation suture passed through the sacral promontory and right anterior sacro-iliac ligament.

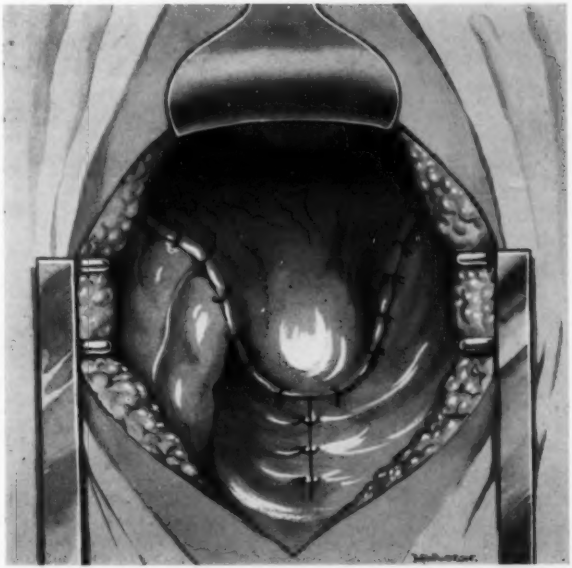

FIG. 3

Peritonization completed, showing restricted access to the pouch of Douglas.

A STUDY OF THE SERUM PROTEIN CHANGES IN PREGNANCY AND TOXAEMIA, USING PAPER STRIP ELECTROPHORESIS

BY

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INTRODUCTION

THE serum protein changes occurring in pregnancy have been studied by the method of paper electrophoresis by Paton, Robertson and Wellby (1954), Brown (1954), and von Stüdnitz (1955). As their findings are not in complete agreement, we felt that the publication of a similar study done in this hospital would be of value.

METHOD

Paper Strip Electrophoresis

The inverted V apparatus as suggested by Flynn and de Mayo (1951) and Whatman No. 1 filter paper were employed. The electrophoretic buffer consisted of 1·03 grams per cent of sodium diethylbarbiturate and 0·184 grams per cent of diethyl barbituric acid. Each electrophoretic strip was run in the apparatus for 18 hours at 150 volts, and then dried rapidly in a current of warm air. The strips were stained with azocarmine B (Gurr) by the method of Plückthun and Götting (1951). Each batch of dye was checked for stability when made up into solution and for constancy of composition by using paper chromatography with a butyl-acetic-water solvent (5.1.4) (Franglen and Martin, 1954). Each stained strip was then interpreted by a reflecting photo-densitometer (Latner, Molyneux and Rose, 1954). This instrument, with a triangular wedge, does not give a linear relationship between the amount of dye present and the amount of protein present. This error was corrected by using the type of instrument since suggested by Latner in 1955. In order to convert each protein fraction into grams of protein the correction factors as suggested by Loeffler and Wunderly (1953) were used.

The total protein was determined by the Micro-Kjeldahl method.

MATERIAL

It was hoped to follow the serum protein changes of 25 healthy women throughout the course of pregnancy, the samples being taken at each antenatal attendance. We were forced to be content with 13 cases, and only one of these 13 attended all her antenatal appointments; the others either missed one or two attendances or declined to give further samples. In each of the latter cases another volunteer at the same stage of pregnancy was substituted. The 21 cases of toxaemia were obtained from the maternity wards of this hospital.

RESULTS

The results in Table I are in the form of percentage of dye present; they are not strictly comparable because the total protein varies during pregnancy. Thus for comparison we converted our figures into grams of protein per cent (Table II). The conversion is based on the assumption that the differential uptake of dye by the various protein fractions is constant for different individuals throughout the course of pregnancy.

The total serum proteins (Micro Kjeldahl) fell during the middle period of pregnancy from 7·3 grams to 6·6 grams per cent (Fig. 1). The serum albumin (electrophoresis) decreased from 4·63 grams per cent at the start of pregnancy to

TABLE I
Serum Protein Changes in Pregnancy

	Normal Values	Normal Pregnancy				Abnormal Pregnancy	
		8–16 Weeks	16–24 Weeks	24–32 Weeks	32–40 Weeks	Hypertension 32–40 Weeks	Toxaemia 32–40 Weeks
Albumin	66·8±4·7	60·7	61·0	53·6	54·7	54·2	49·4
α_1 Globulin ..	2·9±0·9	3·6	4·2	4·9	5·4	5·2	5·9
α_2 Globulin ..	6·4±1·4	8·2	8·6	10·7	10·7	9·6	12·1
β Globulin ..	10·3±1·6	11·7	11·8	15·8	15·8	17·0	18·5
γ Globulin ..	13·7±3·0	15·8	14·6	15·0	13·4	14·0	14·1
Total protein ..	7·3	7·3	6·8	6·6	6·6	6·0	5·7
Number of cases ..	100	13	13	15	13	3	21

Method: Paper strip electrophoresis.
Dye: Azocarmine B.
Units: Percentage of dye present.
By toxaemia is meant pregnancy complicated by hypertension, oedema and albuminuria (Bastiaanse).

TABLE II
Serum Protein Changes in Pregnancy

	Normal Values	Normal Pregnancy				Abnormal Pregnancy	
		8–16 Weeks	16–24 Weeks	24–32 Weeks	32–40 Weeks	Hypertension 32–40 Weeks	Toxaemia 32–40 Weeks
Albumin	4·63±0·33	4·20	3·91	3·34	3·34	3·01	2·57
α_1 Globulin ..	0·24±0·06	0·29	0·32	0·35	0·39	0·34	0·36
α_2 Globulin ..	0·52±0·10	0·65	0·65	0·78	0·77	0·62	0·75
β Globulin ..	0·93±0·11	1·01	0·95	1·21	1·25	1·23	1·25
γ Globulin ..	0·98±0·21	1·15	0·97	0·92	0·85	0·80	0·77
Total protein ..	7·3	7·3	6·8	6·6	6·6	6·0	5·7
Number of cases ..	100	13	13	15	13	3	21

Method: Paper strip electrophoresis.
Dye: Azocarmine B.
Units: Grams of protein per cent.
By toxaemia is meant pregnancy complicated by hypertension, oedema and albuminuria (Bastiaanse).

3·34 grams per cent by the seventh month, and then remained unaltered for the rest of the pregnancy (Fig. 1).

The cases of toxaemia differed from that of normal pregnancy in that their values for total serum protein and serum albumin continued to fall during the last 3 months of pregnancy instead of remaining static (Fig. 1).

The α_1, α_2 and β globulin fractions increased gradually throughout pregnancy (Fig. 2).

The γ globulin fractions rose by an amount statistically insignificant, 0·17 grams per cent, during the first 3 months, and then fell by double this amount during the last 6 months (Fig. 2). In the cases of toxaemia the γ globulin values were lower than in normal pregnancy.

STATISTICAL SIGNIFICANCE

The significance of the difference between two means can be assessed by the ratio of the difference between the two means over the standard error of the difference between them.

When this ratio is equal to 2 then there is a 1 in 20 chance of the difference not being

significant, when $2\frac{1}{2}$ a 1 in 80 chance, when 3 a 1 in 370 chance, etc. (Hill, 1948).

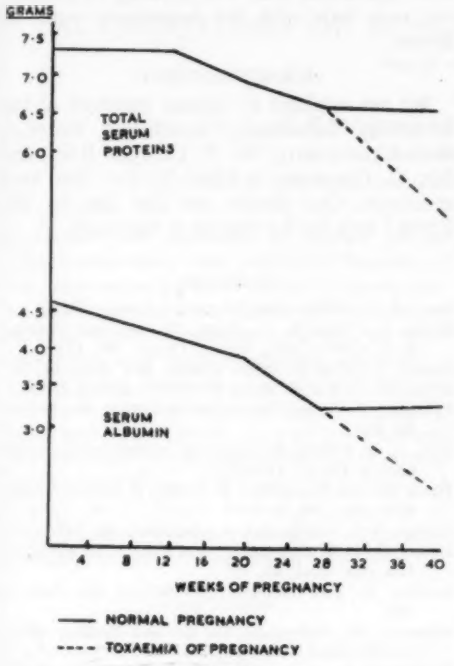

FIG. 1

Serum protein and serum albumin changes in pregnancy.

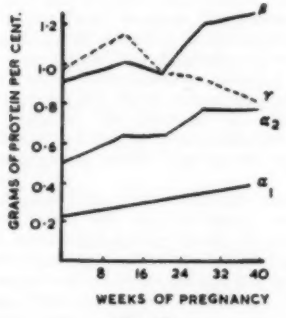

FIG. 2

Serum globulin changes in pregnancy (Units: grams of protein per cent).

The ratios that we obtained for the changes that we observed were as follows:

Serum Albumin	7·8
α_1 Globulin	5·4
α_2 Globulin	4·4
β Globulin	4·6
γ Globulin	2·0

The initial rise of the globulin fraction had a ratio of 1·6, the subsequent fall a ratio of 3·4.

Thus the overall changes that we observed had a statistical significance, except for the initial rise of the globulin fraction.

DISCUSSION

Hoch and Marrack (1948) reviewed the total serum protein changes during pregnancy. They concluded that the majority of writers found a decrease of up to 10 per cent during the first 7 months, and that this decrease is halted or even reversed during the last 3 months. Our findings are similar. These changes must be partly related to the plasma volume which increases by about 1 litre during the first 7 to 8 months, and then falls by about a fifth of a litre during the rest of the pregnancy (Berlin *et al.*, 1953).

The changes of each individual protein fraction have been studied by the method of paper strip electrophoresis by Paton *et al.* (1954), Brown (1954) and von Studnitz (1955).

Paton *et al.* (1954) in Australia reviewed 208 separate estimations. They left their results in the form of a percentage dye present. At this level their findings are in close agreement with ours, except that their normal value for the β globulin reaction is 1·8 per cent lower.

Von Studnitz (1955) in Sweden reviewed 101 separate estimations. His results are in the form of grams of protein and differed from ours principally in that the magnitude of the changes that he observed is less. For example, during the course of pregnancy the serum albumin of his series fell by 0·84 grams per cent, whilst in ours it fell by one and a half times this amount. We were also in disagreement with regard to the exact nature of the changes of the β and γ globulin fractions. These differences were probably due to the difficulty of converting results into grams of protein. Von Studnitz does not state the dye he uses or the correction factors

he applies in order to convert his results into grams of protein.

Brown (1954) reviewed 30 estimations. His findings are left in the form of percentage of dye present, and are at variance with those of Paton and ourselves. Since his paper is only a preliminary report we must await his final conclusions.

The serum protein pattern of 21 cases of toxaemia differed from that of normal pregnancy by lowered values for the serum albumin and γ globulin. These lowered values for the serum albumin did not seem to be related to the degree of proteinuria. For example, one patient had a proteinuria of 0·1 grams per cent with a serum albumin of 2·1 grams per cent and another had a proteinuria 22 times as great yet with a serum albumin of 2·6 grams per cent.

Summary

The serum protein changes in pregnancy and toxaemia were investigated by the method of paper electrophoresis. Our findings were:

(1) The total serum proteins and albumin fell during the first 7 months of pregnancy.

(2) The α_1, α_2 and β globulin fractions steadily increased throughout pregnancy.

(3) The γ globulin fraction fell during pregnancy.

(4) In toxaemia the serum albumin and γ globulin values were lower than in normal pregnancy.

When comparing our findings with those of other writers we found good agreement between ourselves and the work of Paton of Australia; some agreement with von Studnitz of Sweden, but very little with the preliminary work of Brown.

Acknowledgments

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ACTINOMYCOSIS OF OVARIES AND FALLOPIAN TUBES

Report of a Case

BY

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RELATIVELY few accounts of female genital actinomycosis have been published. Records of such cases occurring in the British Isles are rare. The case reported from Edinburgh by Stewart and Muir (1893) appears to have been the first. Berry Hart, also from Edinburgh, described a case of pelvic actinomycosis in 1902. Further reports were published by Thompson (1907), Taylor and Fisher (1909), Shaw (1910), Coté and Tudhope (1936), Armitage and Smith (1954) and MacCarthy (1955). The case here described occurred in Northern Ireland and is one of bilateral tubo-ovarian abscesses probably secondary to infection of the pelvic colon.

CASE HISTORY

The patient, a married woman aged 39, first attended the gynaecological out-patients' department of the Royal Victoria Hospital, Belfast, on 6th January, 1956. She had been married 14 years and had one child aged 7 years. She gave a history of 3-weeks painless vaginal bleeding following 5-months amenorrhoea. About 5½ months previously the patient, on account of pyrexia, lower abdominal pain and diarrhoea, had been admitted to the Northern Ireland Fever Hospital, Purdysburn, Belfast, as a suspected case of dysentery. Bacteriological investigation did not confirm this diagnosis. As the pyrexia persisted all usual investigations including X-ray of chest, barium meal and blood culture were carried out and were negative. The Mantoux test 1/1,000 was positive. Following a course of penicillin, however, her temperature gradually settled and she left hospital on 14th October, 1955.

Clinical Findings. The patient was pale (haemoglobin 56 per cent Sahli) and had obviously lost weight. Abdominal examination did not reveal any abnormality. On gynaecological examination the uterus was in good position, mobile and about normal size but rather softer than normal. Through the left fornix was felt a firm swelling which seemed to be attached to the uterus and suggested a broad ligament fibroid. The cervix showed evidence of chronic infection and erosion. Ten days later, on 16th January, 1956, she was admitted to the gynaecological unit of the Royal Victoria Hospital. On the routine re-examination after admission the cervix was found to bleed easily after contact with the examining finger. In view of this, the patient was examined under anaesthesia the following day. A biopsy of the cervix was taken and curettage performed. On this occasion the uterus was found to be only moderately mobile and bulky with a firm mass attached to each side of it. Some thickening was present in both fornices. A provisional diagnosis was made of fibroids associated with either chronic inflammatory disease or endometriosis. Bearing in mind the past history of pyrexia and pain, the possibility of tuberculous salpingitis was considered but the degree of mobility was such that the presence of tubo-ovarian abscesses was thought to be unlikely.

Histological examination of the endometrium showed the presence of cystic hyperplasia. The cervix was chronically infected but there was no evidence of malignant change. The patient was discharged on 21st January, 1956, with instructions to return for hysterectomy in 6 weeks.

On re-admission on 2nd March, 1956, it was clear that her general condition had deteriorated and she had obviously lost weight. Her temperature was 99·4° F. Blood examination showed a normochromic anaemia and a polymorphonuclear leucocytosis of 11,000. A catheter specimen of urine contained albumin and pus cells and *Bacterium coli* organisms were grown on culture. This urinary infection responded rapidly to a 6-day course of sulphatriad. Transfusion of packed cells raised the haemoglobin to 71 per cent (Sahli).

Laparotomy through a midline sub-umbilical incision was carried out on 14th March, 1956. The uterus was found to be bulky but otherwise appeared normal. Adherent to it were bilateral tubo-ovarian abscesses. Small bowel was attached to the back of the uterus and the right Fallopian tube and ovary. The pelvic colon was thickened and oedematous and bound down to the left tubo-ovarian mass and fundus of uterus. The appendix was lying free on the inner side of the caecum and appeared quite normal. A difficult dissection followed. Adherent bowel was eventually separated from the tubo-ovarian masses which were then mobilized and removed. Considerable oozing occurred. Transfusion of one pint of whole blood was started towards the end of the operation.

As a prophylactic measure against development of paralytic ileus oral feeding was disallowed for the first 48 hours. During this period fluid and electrolyte balance were maintained by intravenous infusion. Penicillin, ½ mega units twice daily, and streptomycin ½ g. twice daily, were given.

The pathological report was as follows: "Both ovaries and tubes are occupied by an inflammatory mass of tissue which histologically consists of multiple abscesses poorly walled off by fibrous tissue. There are clumps of organisms in the centre of these consisting of mycelial filaments and clubs indicating that the infection is of an actinomycotic nature" (Fig. 1).

On receipt of this report the dosage of penicillin was increased to 2 mega units daily and this was continued for 1 month. Streptomycin was discontinued. The patient's post-operative progress was surprisingly smooth. She was discharged from hospital on 14th April, 1956, feeling well and looking considerably improved. A barium enema and sigmoidoscopy carried out shortly before discharge did not reveal any abnormality.

Follow-up. The patient was seen 1 month later, on 14th May, 1956. Her general condition showed further improvement and she had gained 2 stones in weight. The haemoglobin was 80 per cent (Sahli). On gynaecological examination the uterus was normal in size and surprisingly mobile. Three weeks later, on 4th June, 1956, she was re-admitted with vomiting and lower abdominal pain. A tender mass was palpable above the right inguinal ligament and it was clear that the infection had become active again. Penicillin was re-started, 2 mega units being given daily. A good response followed this treatment. All tenderness had disappeared within a week's time. By the end of a month the mass was no longer palpable. She was discharged on 13th July, 1956, to continue the course of penicillin at home for a further 2 weeks. On 4th September, 1956, she was re-examined and found to be in excellent health.

Discussion

Reviews of the literature on actinomycosis of the female genital organs have been published by Cornell (1934), Daniel and Mavrodin (1934) and more recently by Paalman, Dockerty and Mussey (1949) who found 109 cases and added a further 8 of their own from the Mayo Clinic. MacCarthy (1955) was able to collect a total of 157 cases.

The actinomycotic fungus is a normal inhabitant of the mouth and intestinal canal. Colonies of actinomyces have been frequently found in tissue removed at tonsillectomy. The pathogenic anaerobic strains (actinomyces) require culture to distinguish them from the saprophytic aerobic strains (nocardia). Pathogenicity of actinomyces is low. The fungus is unable to penetrate intact mucosa and it is generally believed that infection arises only after a breach in continuity of the mucosa has occurred.

Originally, infection was considered to be commonest in country folk and resulted from chewing or coming into contact with infected grass or grain. In support of this view a case described by Giordano (1895) and one by Daniel and Mavrodin (1934) have been quoted. In the latter case the blade from a barley spike was found in the ovary, having transversed the intestinal wall. Today, the classical origin of infection is no longer generally accepted as accurate. There is very little evidence to suggest that grass or grain is ever infected with pathogenic actinomyces. Also, many of the reported cases have occurred in those living in towns. Paalman's (1949) review does not substantiate the idea that chewing cereals or contact with infected animals or patients is of aetiological importance.

Daniel and Mavrodin (1934) give the order of frequency of infection of the various parts of the genital tract as ovary, ovary and tube, parametrium, uterus, vulva and, least common of all, tube alone. In Paalman's (1949) 109 cases the disease was confined to the right tube and ovary in 37·8 per cent and to the left tube and ovary in 17·8 per cent. In the remaining 44·4 per cent the infection was bilateral. Involvement of the uterus is uncommon. In a total of 157 cases of genital tract infection MacCarthy (1955) found the uterus to be involved in 14. In only 1 case (Neuhauser, 1907) was endometrial infection specifically mentioned. MacCarthy's own case also showed endometrial involvement.

Primary infection of the genital tract is rare and difficult to prove conclusively. In Daniel and Mavrodin's (1934) series of 77 cases 10 were said to be primary, of which 3 were vulval. The primary site of infection was thought to be the cervix in cases described by Mitra (1924), Jaffé (1937) and Campbell and Greaves (1939). Infection following abortion is suggested by cases reported by de Faria and Fialho (1937) and Junghans (1934). The latter writer was able to trace 4 similar cases in the literature. The provision, by trauma, of a portal of entry for the fungus appears to have been present in cases described by Barth (1928) and Tietze (1930) who

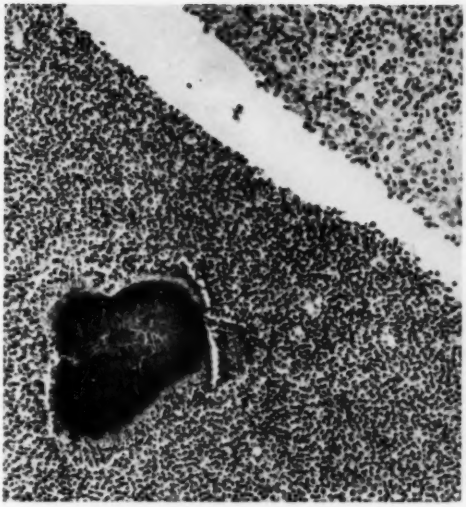

FIG. 1

Photomicrograph showing a "sulphur granule" lying in pus in an abscess in the tubo-ovarian mass. Above and to the right of the cleft a granulomatous reaction is seen. This surrounds the abscess. Foam cells are seen in moderate numbers. H. & E ×125.

describe uterine infection following the use of an intra-uterine contraceptive pessary called a "Sterilette".

Most cases of genital tract actinomycosis, however, are considered to be secondary to intestinal infection. It is thought that escape of the fungus into tissue spaces or peritoneal cavity follows a lesion of the bowel such as appendicitis, perforated duodenal ulcer or diverticulitis. Direct spread to the internal genital organs then occurs. A lesion of the bowel cannot be demonstrated in all cases. Brickner (1925) considered that the organism was able to pass through the intestinal wall without causing any lesion, while Blasek, quoted by Jaffé (1937), felt that the original lesion in the gut may have healed before pelvic genital disease becomes manifest.

The usual primary site of infection is the ileocaecal region. According to MacCarthy (1955) 91 per cent (144 out of 151) of recorded cases have been attributed to an infected appendix. This would account for the frequency of involvement of the right ovary and tube. Those cases in which the left adnexa are involved first are presumably infected from the colon. This is the likely route of extension in the present case in view of the findings at operation and the original history of diarrhoea and abdominal pain. As previously mentioned the appendix appeared perfectly healthy.

The question of diagnosis of pelvic actinomycosis is a difficult one. The clinical features resemble those of chronic pelvic inflammatory disease from other causes, but especially tuberculosis, since fever, loss of weight and anaemia are customary findings. The cases described by Hart (1902) and Robinson (1919) were thought to be tuberculous in origin. On account of the rarity and similarity to the more common pelvic inflammatory conditions it is not surprising, therefore, that a pre-operative diagnosis of actinomycosis of the internal genital organs is seldom made. The possibility of an actinomycotic infection should be borne in mind when a persistent sinus follows operation. Even at the time of operation the true nature of the lesion generally remains obscure or is wrongly diagnosed. The disease may present as an inflammatory mass which has been mistaken for a carcinoma. Ahlström (1930) reported a case in which operation was abandoned as the condition was recorded as malignant. Nine months later the abdomen was re-opened and a pan-hysterectomy performed. The correct diagnosis was only revealed on histological examination.

Treatment

Although spontaneous cure has been described (Armitage and Smith, 1954) a fatal outcome is probable without treatment. Even in fully treated cases the prognosis was poor before the introduction of antibiotic drugs. This applies equally to cases of infection of the female genital tract. Thus 60 per cent of Paalman's 102 cases died. Of Daniel and Mavrodin's 66 cases only 10·6 per cent (7) were cured. The advent of antibiotics, however, brought about a definite improvement. The case described by MacCarthy (1955) received aureomycin and is only the second of the reported cases of genital infection from the British Isles to survive.

Before the introduction of antibiotics many forms of medical treatment either singly or in combination had been used at one time or another and an account of these is given by Paalman *et al.* (1949). They included potassium iodide, which undoubtedly had a beneficial effect, yatren, thymol, vaccines, deep X-rays and sulphonamides.

Favourable reports from the use of penicillin in clinical actinomycosis have been reported by Herrell (1944), Nichols and Herrell (1948), Walker and Hamilton (1945), Jones and Brownell (1945), Sanford and Barnes (1949), Putman, Dockerty and Waugh (1950), and Armitage and Smith (1954). Torrens and Wood (1949) reported satisfactory results in 3 cases treated with streptomycin. Aureomycin has been successfully used by Wright and Lowen (1950), McVay *et al.* (1950), Grant (1951), and Kelly (1951). Littman, Paul and Fusillo (1952) obtained a cure with chloromycetin.

Garrod (1952) found 12 strains of *Actinomyces israelii* to be sensitive *in vitro* to 5 antibiotics. Penicillin was the most effective in inhibiting growth of the fungus, followed by terramycin, chloromycetin, aureomycin and finally streptomycin. In view of these findings and the fact that penicillin is the least toxic of the antibiotics it seems reasonable to give penicillin in the first

instance, more especially as many reported cases have responded satisfactorily to this drug. It should be remembered, however, that not all cases respond to penicillin and if improvement does not occur or fails to be maintained then an alternative antibiotic should be selected.

A good review of treatment of actinomycosis with antibiotics has been published recently by Armitage and Smith (1954). These authors give credit to Nichols and Herrell (1948) for being the first to point out that large doses over a prolonged period are necessary. The generally advocated course of penicillin is 2 mega units daily for 2 months. For a number of reasons the writer's case received 2 mega units for 1 month only. The fact that a relapse occurred within 7 weeks of discharge from hospital would support the view that at least a 2-months course of treatment is required.

Of equal importance is the surgical aspect of treatment. Most authors agree with Brickner (1925) who laid stress on the need for complete excision of diseased tissue whenever possible. This principle can probably be modified now that antibiotics have proved to be effective against the fungus. Cope (1949) considers that the role of surgery is diminishing. Abscesses still require to be drained but the fibrous masses typical of this disease need no longer be excised (Cope, 1949). In genital actinomycosis radical surgery is still probably necessary in many cases. However, with further experience it may be found that less radical measures will be sufficient to bring about a cure. This is particularly desirable in the case of younger women.

Measures designed to improve the patient's general condition and raise her resistance to infection form an important part of treatment. As anaemia and loss of weight are frequent findings in these cases they should be corrected, if possible, before operation is undertaken.

Finally, the incidence of recurrence is high and it is necessary to follow up such cases at regular intervals for a number of years before pronouncing a final cure.

Summary

(1) A case of actinomycosis of ovaries and Fallopian tubes, probably secondary to infection of the pelvic colon, is presented.

(2) Actinomycotic infection of the female genitalia is rare. Only 11 recorded cases from the British Isles have been found.

(3) The prognosis in such cases was poor before the introduction of antibiotic drugs but the outlook has improved considerably.

(4) Penicillin is effective in many cases and it is considered the drug of choice in the first instance. A dose of 2 mega units daily for 2 months is recommended.

(5) Surgery still plays an important part in treatment.

(6) Relapse is common and the need for careful follow up over a number of years is stressed.

(7) The literature is briefly reviewed.

Acknowledgments

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BIRTH WEIGHTS AND PLACENTAL WEIGHTS IN PRE-ECLAMPSIA

BY

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IT is commonly held that pre-eclampsia and essential hypertension tend to be associated with depression of foetal growth, presumably as a result of "placental insufficiency". For example, Morris, Osborn and Wright (1955) state that in severe early pre-eclampsia the development of the foetus "is always retarded and it remains grossly undersized"; and that "the placenta is almost always very small, infarcted, seemingly underdeveloped, and of poor function". We have not traced any reports confirming such impressions statistically. Clinical impressions may be misleading since so many cases of pre-eclampsia and hypertension are delivered prematurely and the "normal" range of birth weights at any stage of gestation varies so widely.

METHOD

The present analysis is based upon 7,168 single births to booked married city primiparae delivered in the Aberdeen Maternity Hospital during the years 1948–55; these hospital cases comprise nearly 90 per cent of all first births in the city. It is not easy to prepare objective statistics relating to pre-eclampsia, owing to uncertainties of diagnosis, especially in mild cases. For present purposes, criteria based on those of Nelson (1955) have been used. Pre-eclampsia is defined as a condition in which the diastolic blood pressure rises, after the 26th week of pregnancy, to 90 or more on two or more occasions separated by at least a day, or shows a definite or progressive pattern if the rise occurs in labour. Severity is assessed in accordance with the presence or absence of albuminuria (catheter specimen of urine). In this series, three grades of severity have been distinguished: (*a*) "severe", when albuminuria rose to 2 g./litre (Esbach) or more; (*b*) "moderate", when albuminuria was present but never rose to 2 g./litre; (*c*) "mild", when there was no definite albuminuria. Oedema is not considered in the diagnosis or the grading. With these criteria, experience has shown that independent assessors obtain virtually identical results when analyzing the same hospital records, there being little room for the exercise of "judgment". While their validity might in some instances be argued, there is no doubt that, generally speaking, the assessment of pre-eclampsia on such lines gives results which seldom conflict with clinical assessments made on more general grounds.

The following cases were excluded from the analysis:

(1) Macerated stillbirths.

(2) Cases (971) in which the duration of gestation was uncertain because the patient was unsure of the date of her last menstrual period, or there was an obvious discrepancy in the first half of pregnancy between the stated date and such phenomena as the growth of the uterine fundus and the start of movements. An unusual birth weight was not, by itself, a reason for rejecting an otherwise acceptable date of last menstruation.

Birth and placental weights in cases of pre-eclampsia were plotted on charts on which lines showing the average (median) and upper and lower extremes for all births at each stage of gestation had already been drawn. If the weights

in pre-eclampsia were abnormally low, the scatter would show an excess of points below the average line and towards the lower limit of the range.

Results

The figure shows the scatter obtained for birth weights in 131 cases of severe pre-eclampsia where the duration of gestation was

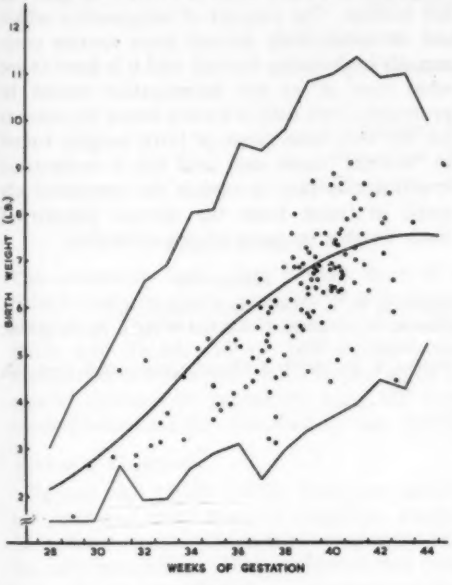

FIG. 1

Birth weights in cases of severe pre-eclampsia. The lines show the upper and lower limits of birth weight and the average (median) birth weight at each period of gestation in all booked primiparae.

reliably established. Before term the majority of weights are below average. After term, the distribution shows no obvious bias.*

* The average birth weight in these 131 cases of severe pre-eclampsia was 5·98 pounds (2·72 kg.). The 971 records rejected owing to uncertainty of gestation period included 21 cases of severe pre-eclampsia with an average birth weight of 5·45 pounds (2·48 kg.), the average gestation period probably being somewhat shorter than in the cases shown in the figure. The bias shown in the figure is not due to the exclusion of cases of pre-eclampsia with relatively high birth weights at the shorter lengths of gestation. More refined methods of analysis show that the bias is not due to differences of maternal size or sex of the baby (Billewicz, 1955).

Similar scatter diagrams for birth weights in pre-eclampsia of mild and of moderate severity show no evidence of abnormal distribution at any stage of gestation. The scatter in cases of essential hypertension (admittedly rather few in number) likewise showed no evidence of bias except when severe pre-eclampsia was superimposed. In such cases the scatter resembled that in severe pre-eclampsia without underlying hypertension, as in the figure.

In severe pre-eclampsia the placental weight was less affected than the baby's birth weight, though the general pattern was the same. That is to say, placentae in cases of severe pre-eclampsia delivered prematurely were usually smaller than "normal" but tended to be relatively large in relation to birth weights.

Discussion

The data show that depression of birth or placental weight in pre-eclampsia is by no means general: a tendency to unusually low birth weights was found only in cases of severe pre-eclampsia in which delivery took place before term. There was no difference in this respect between cases where labour was induced as compared with those in which labour began spontaneously. Though the data are not presented, the results obtained in primigravidae admitted to hospital in emergency owing to pre-eclampsia were practically identical with those found in booked cases.

It was thought that in those cases where the birth weights were low the pre-eclampsia might have been of longer duration than in cases where birth weights were more or less normal for the length of gestation. This was tested by noting the stage of pregnancy at which a diagnosis of pre-eclampsia might first have been made, either in terms of rising blood pressure, or the appearance of oedema. The length of time from this stage until delivery was taken as the duration of symptoms. The average duration of symptoms in cases of low birth weight was longer than in those with a "normal" birth weight, but the difference was small. Further, there were many anomalous cases, for example unusually low birth weights in association with pre-eclampsia of fulminating onset and short duration before termination, or "normal" birth weights (in

relation to the length of gestation) when severe symptoms had been present for several weeks before termination. It seemed impossible to generalize from the data available.

Since foetal mortality from pre-eclampsia is unduly high at extremes of age in primiparae (Nelson, 1955), the birth weight data were plotted so as to distinguish age-groups. It did not appear that maternal age is a factor in deciding whether the birth weight in pre-eclampsia will be "normal" or otherwise.

There is little doubt, from clinical experience, that in some cases of prolonged hypertension during pregnancy, not necessarily of mounting severity, the foetus seems to stop growing normally and eventually becomes liable to sudden intra-uterine death. In such cases, great judgment is necessary to decide whether to allow the pregnancy to continue in the hope that the foetus will become larger, or to induce labour in order to avoid intra-uterine death. The present analysis indicates, however, that such cases are the exception rather than the rule.

We are unable to suggest why the chances of the baby being smaller than average are increased only in cases of pre-eclampsia with marked albuminuria, in which labour begins before term, either spontaneously or after induction. It is particularly difficult to understand why, in such cases, foetal growth should have been depressed when the onset of hypertension has been of short duration, and when the placental weight/birth weight ratio is at least as great as the average. The amount of information which can be consistently derived from routine case-records is obviously limited, and it is hard to see what type of *ad hoc* investigation would be profitable. Very little is known about the reasons for the very wide range of birth weights found in "normal" cases, and until this is understood it will not be easy to explain the comparatively small deviation from the normal pattern of birth weights in cases of pre-eclampsia.

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GASTRIC SECRETION IN PREGNANCY

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INTRODUCTION

THE commonly held view is that there is a reduction in the gastric secretion of acid during pregnancy. This has recently been questioned by Clark and Tankel (1954). The present communication is concerned with a further study of gastric secretion in pregnancy using the augmented histamine test described by Kay (1953).

Review of Literature

Strauss and Castle (1932), using an alcohol test meal and small doses of histamine, studied 24 normal women throughout pregnancy and the early puerperium. They concluded that there was a 50 per cent decline in the maximum free acidity of the gastric contents from the third to the sixth month of gestation with a rise in the last month to the level observed in the third month. After delivery the free gastric acidity was higher than at any time during pregnancy.

Goodall and Gottlieb (1936) performed 115 gastric analyses in a group of women of whom 60 were pregnant and 55 were in the early puerperium. Each individual was studied under basal conditions and one hour after the ingestion of toast and tea; no histamine was used. In the first trimester more than one third showed hypochlorhydria and slightly less than 10 per cent had achlorhydria. Within one week of delivery more than three-quarters of the patients showed a return of acidity.

Low gastric acidities during pregnancy have been reported also by Nakai (1925), Arzt (1926), Mason (1931) and Way (1945). Nakai suggested that the apparent hypochlorhydria was not caused by deficiency of secretion, but resulted from the neutralization of acid by alkaline salts regurgitated from the duodenum. This was disputed by Strauss and Castle (1932) and Way (1945), because they found bile in only very few of their specimens of gastric juice.

While most reports have described hypochlorhydria in pregnancy Labate (1939), working in New York, studied 56 women, nine-tenths of whom were in the last trimester and found that if alcohol was used to stimulate secretion a normal acidity was found in three-quarters of them. Sixteen per cent showed complete post-histamine achlorhydria. It is interesting to note however that 2 women observed to have hypochlorhydria during the twentieth and thirty-second week respectively developed normal concentrations of hydrochloric acid later in the pregnancy, the former at 32 weeks and the latter at 34 weeks. The group of 42 women with normal gastric acidity had an average maximum concentration of free hydrochloric acid of 49 mequiv/l.

Way (1945), using a fractional test meal without histamine (Dodds and Whitby, 1931), reported that in pregnancy there appeared to be some relationship between free acid in the gastric juice and the amount of anterior pituitary-like hormone secreted in the urine. As the amount of

anterior pituitary-like hormone in the urine increased the gastric acidity decreased. Seven of his group of 63 pregnant women were studied more than once during pregnancy and he noted that the secretion of acid was low in early pregnancy and much higher towards the end of pregnancy.

The weight of evidence suggests that there is some reduction in gastric acidity in pregnancy, but Clark and Tankel (1954) were unable to demonstrate this in their investigation which was particularly well designed to test this point. They used continuous aspiration and histamine acid phosphate in a dose of 0·5 mg. in 105 successive tests in 9 women during and after pregnancy, and showed that there was no significant reduction of basal or histamine induced secretion during pregnancy. It is therefore conceivable that the fall of gastric acidity reported by other workers may have been the result of slowing of gastric emptying with greater dilution of the secretion by the retained test meal rather than the result of a fall in the rate of secretion of acid.

Sandweiss, Saltzstein and Farbman (1939) drew attention to the infrequency of peptic ulcer during pregnancy and the beneficial effect which pregnancy had on the symptoms of ulcer. Clark (1953) examined a group of 400 women with peptic ulcer and found that in nearly 90 per cent the symptoms were in abeyance during pregnancy, but this benefit was generally short lived and within 2 years almost every patient had suffered a recurrence.

We have re-studied gastric secretion in pregnancy and have found that basal secretion and the maximal secretory capacity of the mucosa are reduced during the middle months of pregnancy.

Method

Eighty-eight tests have been performed using the augmented histamine test described by Kay (1953) in which the subject is protected from the extra-gastric effects of large doses of histamine by the prior administration of an antihistaminic. Kay showed that it was possible to evoke from the stomach an apparently maximal output of acid in response to 0·4 mg. of histamine acid phosphate per 10 kg. body-weight. Any further increase in dosage was not followed by an appreciable rise in the output of acid, therefore the response to a 4 body-weight dose (4 B.W.) could be used as an index of the maximal parietal secretory capacity of the gastric mucosa.

In the present experiments histamine acid phosphate was injected subcutaneously in multiples of the usual dose of 0·1 mg. per 10 kg. body weight (1 B.W. dose) each dose being covered by the prior administration of 25 mg. mepyramine hydrogen maleate (Anthisan). Halpern (1948) and others have shown that antihistaminic drugs given parenterally antagonize all effects of histamine save that on gastric secretion, although Ragab, Aziz and Mikhail (1952) reported a reduction in basal gastric acidity in normal persons and in patients with peptic ulcers after the administration of mepyramine hydrogen maleate.

In order to satisfy ourselves on this point the basal gastric secretion of 7 non-pregnant women was examined before and after the intramuscular injection of mepyramine hydrogen maleate. Each subject was investigated on 3 occasions. On the first occasion the injection consisted of normal saline, on the second of 100 mg. of mepyramine hydrogen maleate and on the third of 175 mg. mepyramine hydrogen maleate. From our results we concluded that no significant alteration of basal secretion followed the injection of mepyramine hydrogen maleate.

The method employed for the augmented histamine test followed closely that described by Kay (1953). The essential point in this technique is that continuous gastric aspiration is maintained and provision made for dealing with salivary contamination. We found that to maintain successful aspiration of secretion frequent alteration of the patient's position was required.

Four patients complained of headache following the injections of histamine and many became drowsy and complained of transient nausea after the administration of the larger doses of mepyramine hydrogen maleate. These side effects were short lived. On one occasion there was a serious complication in a patient who was known to have a gastric ulcer. After a 1 B.W. dose of histamine she had a moderate

haematemesis. In 91 separate tests there were 3 technical failures.

The results of gastric analyses must be interpreted with care. The common methods of expressing secretory activity of gastric mucosa are in terms either of concentration of acid in the gastric contents, or as an amount of acid aspirated per unit of time. The amount of titratable acid recovered is not always a reliable index of the amount of acid secreted because it is known that the gastric mucosa secretes a varying amount of fluid containing bicarbonate which neutralizes the acid secretion. Hunt (1953) has shown quantitatively how the fractional test meal technique gives concentrations of acid in gastric contents which vary with the rate of gastric emptying. With a standard secretory pattern the concentration of acid reached in the gastric contents is reduced when the emptying of the stomach is slowed.

Fisher and Hunt (1950) examined the data of Ihre (1938) and showed how human gastric secretion could be divided into two hypothetical components, an acid component having its origin in the parietal cells, and a second component made up of the secretions of other cells in the gastric mucosa. Thompson and Vane (1953), assuming that the parietal component (P) and the non-parietal component equalled the volume of the total gastric secretion (V), derived the formula:

$$P = V\,(0{\cdot}219 + 4{\cdot}88[H+])$$

Where $H+$ = concentration of free acid (mequiv/l)

and V = volume (ml.).

By using this formula the volume of parietal secretion in a sample may be calculated where only the volume and acidity are known.

The Patients

Fourteen pregnant women and 10 non-pregnant women were studied first. The average age in both groups was 25 years. One patient was in the first trimester, 4 in the second and 9 in the last. In these 24 women the test was carried out on three occasions. After the collection of basal secretion over a 45 minute period either a 1 B.W., 4 B.W., or 7 B.W. dose of histamine was given. In some instances the tests were performed on consecutive days but in the majority an interval of several days separated each test.

After the above studies a further group of 16 pregnant women were tested on one occasion only with a 4 B.W. dose of histamine so that there were in all 3 groups of women equally distributed throughout the trimesters of pregnancy. The average age of this final group of 30 pregnant women was 28 years.

The nature of the study was explained to the patients and they took part in this investigation on a voluntary basis.

Results

Our data have been expressed in both milligrammes of total acid (titrated with phenolphthalein to pH 8) and as volume of parietal component based on the concentration of free acid (titrated with Töpfer's reagent to pH 3·5). The use of parietal component minimizes the effect of neutralization of secreted acid by non-acid secretion and gives more consistent results.

Statistical Method

In the discussion of results where it is necessary to compare mean values the figures in parentheses indicate the level of significance of the difference between the means. Thus (1/20) indicates that if in fact there were no differences in the patients tested the observed difference between the means would arise by chance once out of twenty times.

Basal Secretion of Acid in Non-pregnant and Pregnant Women

When the data for basal secretion on three separate occasions from non-pregnant women (Table I) were compared it was found that the mean amount in milligrammes of total acid aspirated on the third occasion was significantly higher (1/50) than on the first occasion. The volumes of parietal cell component based on free acid showed similar trends in the three tests but the differences were not significant.

The nature of the test may explain the lower values obtained on the first occasion during which the subjects were more apprehensive and nausea was more marked. These two factors

TABLE I
Basal Aspirates on Three Occasions from 10 Non-pregnant Women and 14 Pregnant Women

Non-pregnant	First Occasion	Second Occasion	Third Occasion
Mean Total Acid (mg./45 minutes)	44 (±7·3)	65 (±17·1)	81 (±12·3)
	Mean of 30 tests 63 (±7·8)		
Mean Volumes of Parietal Component (ml./45 minutes)	14 (±2·3)	16 (±2·7)	19 (±2·7)
	Mean of 30 tests 16 (±1·5)		
Pregnant			
Mean Total Acid (mg./45 minutes)	86 (±14)	90 (±26)	101 (±27)
	Mean of 42 tests 92 (±13)		
Mean Volumes of Parietal Component (ml./45 minutes)	19 (±3·0)	20 (±4·0)	19 (±3·6)
	Mean of 42 tests 19 (±2·3)		

The figures in parentheses is this and the following tables are standard errors of the means.

possibly contributed to the low values for the first tests partly on account of inhibition of gastric secretion and partly as a result of contamination of the aspirate with saliva. The calculation of volume of parietal cell component minimized the error from contamination and the basal values showed no significant difference from test to test. The rate of basal secretion during pregnancy on three separate occasions when expressed in milligrammes of acid showed slight differences, the first test giving a lower value than the third test but the differences were not significant.

When non-pregnant women and pregnant women are compared no account being taken of the stage of gestation there are no significant differences in the rates of basal secretion (Table I). When the gestational period is considered, the mean rate of basal secretion is reduced in mid-pregnancy (1/50) as compared with early and late pregnancy (Table II) and when the pregnant women are grouped in smaller gestational periods of 10 weeks, and compared with non-pregnant women the depression at the third 10-weekly period is highly significant (1/1,000). The data of 4 of the subjects have been excluded from Table III because 2 women in the second 10-week period and 1 in the third 10-week period, although normal at the time of testing, subsequently developed pre-eclamptic toxaemia at term; the remaining subject was first tested at 27-weeks gestation and it was not possible to repeat the test until 9 weeks later.

Histamine Induced Gastric Secretion

The responses to three different doses of histamine in 10 non-pregnant and 14 pregnant

TABLE II
Basal Aspirates of Acid from 10 Non-pregnant Women and 30 Pregnant Women Grouped Equally in Trimesters

Mean Total Acid (mg./45 minutes)			
Non-pregnant	Pregnant 30 Women		
	First Trimester	Second Trimester	Third Trimester
10 women 30 observations	10 women 12 observations	10 women 18 observations	10 women 28 observations
63 (±7·8)	79 (±20)	36 (±12)	107 (±28)
Mean Volumes of Parietal Component (ml./45 minutes)			
16 (±1·5)	21 (±3·7)	12 (±2·5)	22 (±4·2)

TABLE III

Basal Aspirates of Acid from 10 Non-pregnant Women and 26 Pregnant Women Grouped in 10-Week Periods

Mean Volumes of Parietal Component (ml./45 minutes)				
Non-pregnant	Pregnancy 26 Women			
	First 10 Weeks	Second 10 Weeks	Third 10 Weeks	Fourth 10 Weeks
10 women 30 observations	3 women 3 observations	8 women 10 observations	6 women 12 observations	9 women 27 observations
16 (±1·5)	23 (±4·9)	13 (±2·8)	7·6 (±1·3)	23 (±4·4)

TABLE IV

The Responses to Three Different Doses of Histamine in 10 Non-pregnant Women and 14 Pregnant Women Not Grouped in Trimesters

Non-pregnant	Histamine Acid Phosphate in Doses of 0·1 mg./10 kg. Body-weight (B.W.)		
	1 B.W.	4 B.W.	7 B.W.
Mean total acid (mg./30 minutes)	180 (±29)	360 (±44)	380 (±31)
Mean volumes of parietal component (ml./30 minutes)	30 (±3·6)	61 (±6·8)	64 (±6·6)
Pregnant			
Mean total acid (mg./30 minutes)	210 (±34)	350 (±49)	340 (±55)
Mean volumes of parietal component (ml./30 minutes)	37 (±5·9)	59 (±8·4)	56 (±9·0)

women. Table IV shows that the mean secretory response to histamine is maximal with a 4 B.W. dose since no greater response was obtained from a 7 B.W. dose in either non-pregnant or pregnant women. This confirms Kay's (1953) finding for men. A single B.W. dose of histamine produced about 50 per cent of the maximal response, which is in agreement with Hunt and Kay (1954). Again in this ungrouped data no difference in response between pregnant and non-pregnant women appeared.

The responses to three different doses of histamine in non-pregnant women and pregnant women grouped in trimesters. Of the 14 pregnant women 5 were in the first and second trimesters and 9 in the last trimester.

Table V shows that the depression of response to a maximal stimulus in the first two trimesters of pregnancy when compared with non-pregnant women and pregnant women in the last trimester is significant (1/100).

The responses to a maximal stimulating dose of histamine in non-pregnant women and pregnant women grouped in trimesters and four 10-week periods of pregnancy. Table VI shows the results for the larger group of 30 women arranged in trimesters of pregnancy. In the additional 16 pregnant women examined data was obtained for basal and maximal responses only.

The maximal response in the first and second trimesters was significantly depressed compared with the response in non-pregnant women (1/20). Similar results are shown in Table VII when the 26 patients referred to above are grouped in 10-week periods of pregnancy. The difference in maximal response to histamine between pregnant and non-pregnant women was significant during the first 30 weeks of pregnancy (1/20).

In order to obtain a simple idea of how basal and maximal secretion varied during pregnancy running averages for 6 subjects have been plotted (Fig. 1). The fall in maximal histamine response is clearly shown. The fall in basal secretion was slower and reached its lowest point at a slightly later stage in pregnancy.

TABLE V

The Responses to Three Different Doses of Histamine in 10 Non-pregnant Women and 14 Pregnant Women Grouped in Trimesters

Non-pregnant	Histamine Acid Phosphate in Doses of 0·1 mg./10 kg. Body-weight (B.W.)		
	1 B.W.	4 B.W.	7 B.W.
Mean total acid (mg./30 minutes)	180 (±29)	360 (±44)	380 (±31)
Mean volumes of parietal component (ml./30 minutes)	30 (±3·6)	61 (±6·8)	64 (±6·6)
Pregnant			
First and Second Trimester 5 women:			
Mean total acid (mg./30 minutes)	140 (±35)	190 (±29)	180 (±33)
Mean volumes of parietal component (ml./30 minutes)	25 (±5·6)	31 (±4·9)	31 (±5·4)
Pregnant			
Third Trimester 9 women:			
Mean total acid (mg./30 minutes)	240 (±47)	430 (±57)	430 (±66)
Mean volumes of parietal component (ml./30 minutes)	41 (±7·8)	74 (±9·5)	70 (±11·4)

TABLE VI

The Responses to a Maximal Stimulating Dose of Histamine in Non-pregnant Women and Pregnant Women Grouped in Trimesters

Mean Total Acid (mg./30 minutes)			
Non-pregnant	Pregnancy 30 Women		
	First Trimester	Second Trimester	Third Trimester
10 women	10 women	10 women	10 women
360 (±44)	249 (±30)	262 (±46)	419 (±52)
Mean Volumes of Parietal Component (ml./30 minutes)			
61 (±6·8)	45 (±5·0)	43 (±6·0)	72 (±8·7)

TABLE VII

The Responses to a Maximal Stimulating Dose of Histamine in Non-pregnant Women and Women Grouped in 10-Week Periods of Pregnancy

Mean Volumes of Parietal Component (ml./30 minutes)				
Non-pregnant	Pregnant 26 Women			
	First 10 Weeks	Second 10 Weeks	Third 10 Weeks	Fourth 10 Weeks
10 women	3 women	8 women	6 women	9 women
61 (±6·8)	46 (±11·3)	42 (±7·2)	45 (±6·6)	74 (±9·4)
	Mean 44 (±4·3)			

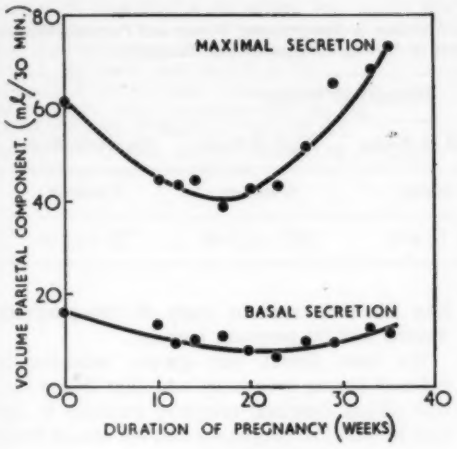

FIG. 1

DISCUSSION

Basal Secretion

Clark and Tankel (1954) showed that in successive tests the mean basal secretion remained constant both during and after pregnancy. In their series of 9 women, 2 had a history of duodenal ulcer and 1 patient developed pre-eclamptic toxaemia. On examination of the individual observations on the remaining 6 women, only 3 showed a very slight depression in mid-pregnancy. In view of this our data for basal secretion for all the women tested were re-examined and the highest values for basal secretion were selected as representing the "best" results. For these data the difference between the non-pregnant women and women in the middle trimester was still significant (1/20).

Histamine Induced Secretion

Clark and Tankel (1954) using a stimulus of 0·1 mg. of histamine per 10 kg. body weight, came to the conclusion that there were no differences in response between pregnant and non-pregnant women to histamine induced secretion. Our results with the same stimulus confirm their findings. However, when a maximal stimulating dose of histamine (0·4 mg. per 10 kg.) was used we observed a significant depression of response in early and mid-pregnancy. We have confirmed in women, pregnant or not, Kay's (1953) findings for normal men that a 4 B.W. dose of histamine produced an apparently maximal secretory response. It should be pointed out that, while the mean values clearly demonstrated that the response to a 7 B.W. dose was no greater than to a 4 B.W. dose, the "plateau" effect described by Kay could not be seen in every individual.

The parietal secretory response to 4 B.W. doses in the first 30 weeks of pregnancy was significantly reduced when compared with that of non-pregnant women and women in the last 10 weeks of pregnancy. This response to maximal stimulation in the first 30 weeks of pregnancy is almost the same as the response to a single B.W. dose in late pregnancy and in the non-pregnant subject. The reason for this alteration in early and middle pregnancy is not known.

Histamine acts directly on the parietal cells of the gastric mucosa. It may be that the alteration of response to histamine is due to the intervention of an anti-histaminic substance. Ahlmark (1944) has shown that plasma histaminase levels may rise a thousand times or more during pregnancy. Rostorfer and Laskowski (1945) using a histaminase preparation obtained from hog kidney were unable to show that histaminase depressed histamine induced secretion in "pouch" dogs. Grossman and Robertson (1948) working with a less toxic histaminase preparation also obtained from hog kidney demonstrated in "pouch" dogs that histamine induced gastric secretion was depressed. They could not decide however whether the inhibition of gastric secretion was due to the histaminase or to some other constituents of the kidney extract. On the other hand Clark and Tankel (1954) were unable to show any correlation between plasma histaminase levels and the gastric secretion of acid.

In the 5 women studied during the first and second trimesters with both 4 and 7 B.W. doses of histamine the mean responses were practically identical. Examination of the individual responses was inconclusive. If histamine were destroyed before reaching the gastric mucosa it could be anticipated that the maximum secretion would occur in response to a higher dose of histamine than 4 B.W. This does not in

TABLE VIII

The Percentage of Maximal Secretory Power Active in Basal Secretion in Non-pregnant Women and Pregnant Women Grouped in 10-Week Periods. Based on Volumes of Parietal Component (ml./30 minutes)

Non-pregnant	Pregnant 26 Women			
	First 10 Weeks	Second 10 Weeks	Third 10 Weeks	Fourth 10 Weeks
10 women	3 women	8 women	6 women	9 women
19 (±2·4)	38 (±12)	24 (±4·7)	12·5 (±3·4)	22 (±3·7)

fact occur. Furthermore the response to 1 B.W. dose of histamine in mid-pregnancy is almost as great as the response to 4 B.W., which is further evidence against the intervention of histaminase in producing the reduced acid response at this stage of pregnancy. Although the number of women examined is small we feel that it is unlikely that plasma histaminase reduces the amount of histamine reaching the parietal cells. The observation that the rate of basal secretion is reduced as well as the response to maximal stimulation suggests that there is either an alteration in the reactivity of the parietal cells or a reduction in the number of functioning cells during pregnancy.

Hunt and Kay (1954) have shown in patients with duodenal ulcer that although both basal and maximal secretion are greatly increased the ratio of the two remains the same as in normal men. Hunt and Kay give the ratio for normal men as 33·7 per cent. Dr. Hunt informs us that this figure was in error and should be corrected to 22·4 per cent (SE±2·2). Our finding for non-pregnant women is 19 per cent (±2·6). The corresponding figures for the various stages in pregnancy are given in Table VIII. Although there is no significant difference between this ratio in pregnant and non-pregnant women there would appear to be a significant depression (1/20) when the third 10-week period is compared with the rest of pregnancy.

The reduction of gastric acidity during pregnancy provides a rational explanation for the disappearance of symptoms of peptic ulcer in nearly 90 per cent of women during pregnancy.

SUMMARY

The augmented histamine test described by Kay has been used to study 10 non-pregnant women and 30 pregnant women.

We have found that gastric secretion is reduced during pregnancy and that this reduction affects maximal secretory capacity in the first 30 weeks of pregnancy and the rate of basal secretion in the middle months of pregnancy.

It is suggested that this alteration is due to a change in the reactivity of the parietal cells of the gastric mucosa. It is unlikely that plasma histaminase interferes with the action of histamine.

ACKNOWLEDGMENTS

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OSSIFICATION CENTRES AS EVIDENCE OF FOETAL MATURITY

BY

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AN estimate of the degree of maturity of a foetus is often required in the management of maternal hypertension, pre-eclampsia, ante-partum haemorrhage, hydramnios and other disorders of pregnancy. In such conditions, roentgenography is of great service, both in the search for signs of foetal malformation and in the estimate of the general degree of ossification, the size of the foetus and the size of the foetal head as indications of the progress of foetal development.

When satisfactory films show details of the region of the knee and ankle joints, the presence and size of the ossification centres provide the radiologist with further evidence for an opinion on the development of the foetus. In our experience, the table of average dates of appearance of ossification centres presented by Chassar Moir (1955) is a valuable guide, particularly in relation to the lower epiphysis of the femur, which appears between the 35th and 40th week, the cuboid which appears between the 36th and 40th week and the upper epiphysis of the tibia which appears at the 40th week. These are described as merely average dates, subject to much individual variation. It may therefore be useful to know the range and variety of appearances which may be expected at maturity and these have been estimated after the radiographic examination of a series of 100 newly-born mature infants.

The cases chosen for this investigation were the apparently normal infants of healthy, normal white women, with, as far as could be ascertained by reliance on the patient's memory, regular menstruation and an accurate date of the last menstrual period and an uncomplicated pregnancy and delivery within three days of the predicted date. Radiographs were obtained shortly after birth. The results are classified below.

RESULTS

Knee Joint

Lower Femoral Epiphysis. This epiphysis was present in 99 of the 100 cases examined and was well developed in 78 cases. In the one case where the epiphysis was absent, the upper tibial epiphysis and the cuboid were also absent. This infant was a male, weighing 3,300 g. (7 pounds 6 ounces).

The analysis of the presence of epiphyses by weight and sex (Tables I and II) confirmed the observation made by Christie (1949) that ossification was more advanced in female than male infants. However, all gradations of epiphyseal size were found in both male and female infants.

The degree of ossification did not, in this small series, vary significantly with weight. In half of the infants weighing more than 8 pounds (3,600 g.), the upper tibial epiphysis was small or absent.

Upper Tibial Epiphysis. This epiphysis was present in 72 of the 100 cases, and was well developed in 39 cases. In no case was it present in the absence of the lower femoral epiphysis.

In about half of the cases where both centres were present, the upper tibial epiphysis, although of somewhat different shape, occupied an area as large as, or larger than, the femoral epiphysis.

TABLE I
Analysis of Epiphyses in Relation to Weight
(Gestation 280 days±3 in all cases)

Weight	Lower Femoral Epiphysis			Upper Tibial Epiphysis		
	Well Developed	Small* 4×3 mm.	Absent	Well Developed	Small 4×3 mm.	Absent
5–6 pounds (2,250–2,700 g.) ..	3	1	–	–	3	1
6–7 pounds (2,700–3,150 g.) ..	18	9	–	9	10	8
7–8 pounds (3,150–3,600 g.) ..	33	5	1	15	11	12
8–9 pounds (3,600–4,050 g.) ..	20	5	–	11	9	6
Over 9 pounds (4,050 g.)	4	1	–	4	–	1

* Measured on the plate.

TABLE II
Analysis of Epiphyses in Relation to Sex

	Lower Femoral Epiphysis			Upper Tibial Epiphysis		
	Well Developed	Small* 4×3 mm.	Absent	Well Developed	Small 4×3 mm.	Absent
Female	41	6	–	22	12	13
Male	37	15	1	17	21	15

* Measured on the plate.

The upper tibial epiphysis was large and well developed with the cuboid centre absent or faint in 33 cases.

Tarsal Bones

Calcaneus and Talus. Ossification was well developed in all cases.

Cuboid. This centre of ossification was absent in 72 cases. Of the remaining 28 cases, the bone was well developed and well calcified in only 13 cases. The variation was from nil to 6 mm. in diameter. In the 15 cases in which the bone was poorly calcified, it was represented by a cluster of small centres. In 5 cases there were 2 centres, in 8 cases 3 centres, and in the remaining 2 cases 4 centres. All cuboid centres above 4 mm. in diameter produced an opacity of uniform density.

When the cuboid was well developed, the lower femoral epiphysis was also well developed. In 3 cases, where the lower femoral epiphysis was poorly calcified and likely to be invisible on radiography before birth, a small cuboid centre of similar density was also observed

In the 13 cases with the cuboid well calcified, the upper tibial epiphysis was absent in 3 cases. The upper tibial epiphysis was absent in a further 3 cases where the cuboid was poorly calcified.

Lateral Cuneiform. In 2 cases, where the cuboid was well calcified and both lower femoral and upper tibial epiphyses were present, another centre of ossification was noted in the tarsus, presumably the centre of the lateral cuneiform bone.

In conclusion, of the 100 cases examined, there was only one case where the lower femoral, upper tibial and cuboid centres were absent, and the birth weight of this infant was 7 pounds 6 ounces (3,300 g.). In 21 cases both the upper tibial epiphysis and the cuboid centre were absent.

DISCUSSION

There is no method available to predict with certainty the maturity of a particular foetus. Observations made in animal breeding point out the range of variation in the conception/delivery interval and support the impression of obstetricians concerning the variation in human gestation time. In this series, the clinical data

were carefully scrutinized and patients were excluded from the series if there was any doubt as to the date of the last menstrual period, if their menstrual cycle had been irregular or if there was any discrepancy between the size of the uterus and the size expected for the duration of amenorrhoea at the time of abdominal and pelvic examinations in early pregnancy. All the pregnancies were uncomplicated and the deliveries took place within 3 days of the date predicted by the usual Naegele method of calculation.

The range of variation of ossification centres has been commented upon by many observers and Adair and Scammon (1921) reviewed the evidence available before this date from post-mortem examinations and radiographs. In their series of 100 newborn infants, the range of apparent gestation time, as calculated from the first day of the last menstrual period in patients with a reliable menstrual history, was 233 to 312 days. Although the two series are not strictly comparable, they do agree in pointing out the variation in the time of appearance of these centres. Christie *et al.* (1941) found in their study of the ossification of the cuboid bone that it was present in 41 per cent of white boys born between the 38th and 41st weeks and in 67 per cent of white girls born at the same gestation time. This higher incidence, which contrasts with our experience, may be due to a greater proportion of these cases occurring in infants delivered after the expected date of delivery.

That the cuboid ossifies from a cluster of small centres has been noted by several authors and is confirmed in this series.

In a survey of roentgenography of 1,112 newborn infants Christie (1949) showed that for any selected centre of ossification in infants of white or Negro race, or either sex, there is a progressive prevalence as the weight at birth increases. This was not a feature of the present study where the weight of the infant was not related to gestation time. It is suggested that all the infants of this series were of the same physiological maturity in terms of gestation time and that the differences found in the ossification centres are physiological variations occurring in normal pregnancy at term.

It appears that absence of any one centre is not incompatible with maturity. Absence of the cuboid may be noted when the lower femoral and upper tibial epiphyses are very well developed. Marked development of any of these centres may be observed in normal maturity and therefore such a finding is not evidence of postmaturity.

Summary

The ossification centres of the cuboid and the epiphyses of the lower end of the femur and the upper end of the tibia were examined in 100 apparently mature infants delivered from healthy mothers within 3 days of the predicted date.

The epiphysis of the lower end of the femur was present in 99 of the 100 cases and was judged to be sufficiently well calcified to be visible by radiography before birth in at least 78 cases.

The epiphysis of the upper end of the tibia was present in 72 of the 100 cases and was well developed and well calcified in 39 cases.

The cuboid was ossified in 28 of the 100 cases and well developed and well calcified in 13 cases. Its multicentric ossification was noted.

The absence of any one centre is not incompatible with maturity and marked development does not, of necessity, mean a prolongation of pregnancy.

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MASSIVE POST-PARTUM HAEMORRHAGE ASSOCIATED WITH AFIBRINOGENAEMIA

BY

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THIS case is one in which, following a cyanotic episode at or just before the commencement of labour, there was a subsequent severe post-partum haemorrhage associated with very low blood fibrinogen levels. The case is thought to be of some interest, both from the point of view of treatment of the condition, and also with regard to the diagnosis of the underlying cause of the afibrinogenaemia.

CASE REPORT

The patient was a married primigravida, aged 19 years, who had attended the Antenatal Clinic at St. Mary's Hospital from about the 8th week of pregnancy. She had had no previous serious illnesses or operations and the expected date of confinement was 20th November, 1956.

She remained well during the pregnancy. The blood pressure did not rise above 120/80 mm. Hg, the urine remained clear and no oedema developed. At about the 37th week of pregnancy she was admitted to hospital because of a radiological report suggesting a Grade II placenta praevia, though there had been no ante-partum haemorrhage. She remained well whilst in hospital, no sign of toxaemia developed, and in view of the absence of clinical signs of placenta praevia it was decided to await the spontaneous onset of labour.

Labour. At about 3 a.m. on the 20th November, the patient was noted by the night nurse to be breathing stertorously and was found to be unconscious and deeply cyanosed. She was seen by the house surgeon five minutes later who lifted up the jaw and gave her oxygen —the cyanosis became much less marked. She began to recover consciousness, became very restless and noisy, and complained of abdominal pain. The uterus was very firmly contracted but not wooden hard. She was given a light anaesthetic of ether, nitrous oxide and oxygen and transferred to the labour ward where she was examined again. She was not cyanosed now, there was no evidence of tongue biting or frothing at the mouth, her pulse was 120 a minute and blood pressure 90/60 mm. Hg. The pupils were equal and reacted to light and there was no evident paralysis of the limbs.

The uterus was firmly contracted, foetal parts were difficult to feel and the foetal heart could not be heard. There was no vaginal haemorrhage but the bed was wet, and this was thought to be due to urinary incontinence.

At this stage it was thought that the patient had had a fit—probably eclamptic with accidental haemorrhage—although no actual convulsion had been witnessed and the blood pressure was low. On this assumption light anaesthesia was continued, morphine sulphate 15 mg. was given intravenously, and a catheter passed which produced only a small quantity of urine containing no albumin.

At about 5 a.m. the uterus was much more relaxed and the foetal parts could be felt. The patient was beginning to recover consciousness.

By 5.30 a.m. regular uterine contractions were occurring, there was a red "show" and the patient was in labour. The foetal heart was now audible. The blood pressure was 110/70 mm. Hg, and the pulse rate 112 per minute.

At 6 a.m. blood was taken for the fibrinogen test; the blood failed to clot in 25 minutes and a quick result of fibrinogen gave a figure of less than 200 mg. per 100 ml.

The patient continued in labour and by 7.30 a.m. was having strong contractions every 3

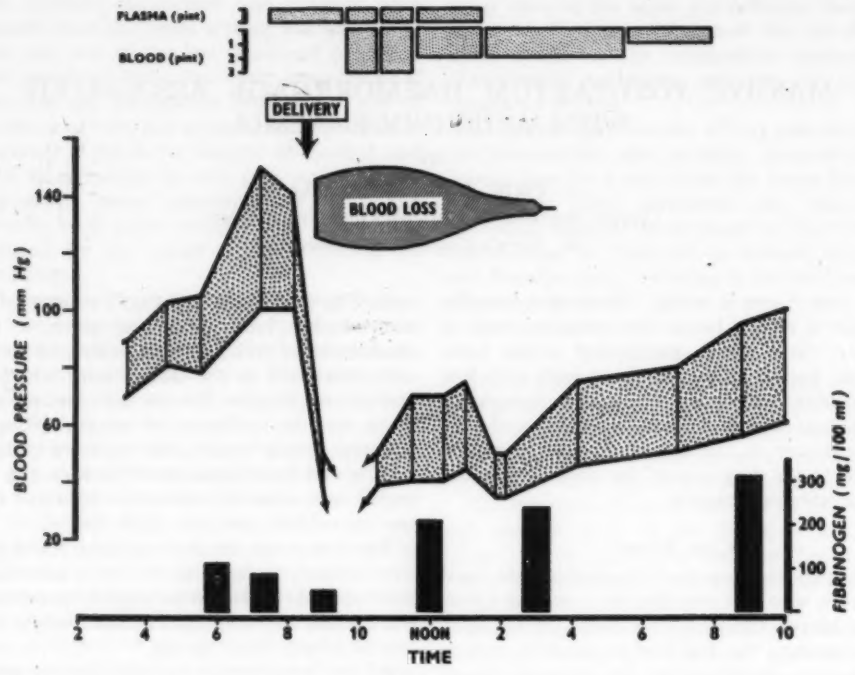

FIG. 1

Diagrammatic record of plasma and blood administration, blood loss, blood pressure and fibrinogen blood level in relation to delivery.

minutes. Her pulse rate was 96, her blood pressure had risen to 150/100 mm. Hg, and a specimen of urine at this time was loaded with albumin.

In view of the low blood fibrinogen report it was decided to give the patient fibrinogen in the form of concentrated plasma, and an intravenous infusion of triple strength plasma (that is the dried contents of 3 bottles of plasma dissolved in 1 bottle of water) was established.

Labour continued normally—at 8.10 a.m. the head was visible and at 8.40 a.m. normal delivery of a living male child took place. The infant weighed 9 pounds 4 ounces, and was somewhat asphyxiated and slow to breathe, but it responded to resuscitation and breathed after 10 minutes.

Following delivery there was an immediate loss of about 2 pints of fresh unclotted blood. Ergometrine ½ mg. was given intravenously, a general anaesthetic was administered, and a manual removal of the placenta carried out. The placenta was about one-third adherent to the upper and anterior wall of the uterus. During this time the blood loss was continuous and the patient collapsed, her pulse was rapid and hardly perceptible and the systolic blood pressure fell to 50 mm. Hg. Blood loss continued in spite of further ergometrine intravenously and bimanual compression of the uterus. There was no laceration of the uterine lower segment or cervix (Fig. 1).

Resuscitation. The patient's condition was now very poor—she was unresponsive, with an impalpable pulse and sighing respirations, and the blood pressure was not recordable.

The first pint of triple strength plasma had been administered and, using a cut-down drip

in the right ankle, whole blood was given rapidly under pressure—3 pints were given in the first hour together with a further pint of triple strength plasma. Oxygen was administered. The uterus was massaged and controlled in the abdomen, and further ergometrine given but a steady blood loss of unclotted blood continued.

By about 10.30 a.m. her condition had not improved, the blood loss was still continuing in spite of a fairly well contracted uterus, and it was decided to pack the vagina and lower uterine segment. Using 3 rolls of 6-inch gauze the vagina and lower segment were thoroughly packed. Blood transfusion under pressure was continued, a further 3 pints of whole blood and another pint of triple strength plasma were administered in the next hour.

Following the vaginal packing and the further blood and plasma her condition improved somewhat and by 11.45 a.m. her blood pressure was recordable at 70/40 mm. Hg and the pulse was palpable.

By midday her condition was much improved; the blood pressure was 75/40 mm. Hg, the pulse rate 144 and the peripheral circulation was returning. The vaginal pack was soaked but she was not bleeding through the pack. A further 2 pints of blood and ½ pint of triple strength plasma were given between 12 and 1.30 p.m.

At 1.30 p.m., in view of the soaked nature of the vaginal pack, she was taken to the theatre and examined there under a general anaesthetic. The uterine cavity was explored and the cervix and vagina inspected. There was no laceration of significance. Following a hot intra-uterine dettol douche at 115° F., the uterus contracted well and the bleeding virtually ceased. A small pack was placed in the uterus and vagina. She was returned to the ward and blood transfusion continued—a further 2 pints of blood were given by 4.30 p.m.

Her condition improved during the afternoon and there was no further bleeding. By early evening (8 p.m.) the blood pressure had risen to 100/55 mm. Hg and at 11 p.m. the transfusion was discontinued. She had received 11 pints of blood, 3½ pints of triple strength plasma and 1 pint of dextrose.

Reconstituted dried plasma is an excellent source of fibrinogen and contains about 0·35 g. per cent of fibrinogen (Scott, 1955). Triple strength plasma is therefore likely to contain about 1 g. per cent of fibrinogen or approximately 4 to 5 g. per pint.

The chart indicates the blood levels of fibrinogen. It is seen that during labour the fibrinogen level was dangerously low (113 mg. at 6 a.m.; 89 mg. at 7.30 a.m.) and at delivery had reached the very low level of 50 mg. per 100 ml. in spite of administration of 1 pint (570 ml.) of triple strength plasma. By 12 noon, when the blood loss had become much less, the fibrinogen level had risen to 206 mg. per 100 ml. and was normal (305 mg.) by 9 p.m. that night. It may also be noted that at 1.30 p.m. there was blood clot in the uterus and this was the first indication of the return of normal clotting power.

Next morning the patient's condition was quite good, her pulse rate was 120 per minute, the blood pressure 100/50 mm. Hg, and the uterine pack was removed without further haemorrhage. The urine output was surprisingly good—first specimen 4 ounces 12 hours after delivery, then 47 ounces in the first 24 hours, and 51 ounces on the 2nd day after delivery.

She was given prophylactic antibiotics but her temperature rose to 100·4° F. on the 2nd day after delivery and there was a low grade pyrexia for 10 days. There was some thrombophlebitis of the internal saphenous vein (the site of transfusion) but this settled down uneventfully.

On the 10th day after delivery her haemoglobin was only 54 per cent and she was given a further 2 pints of blood.

The baby gave cause for anxiety for the first 2 days and had attacks of cyanosis but then recovered well and was breast fed.

Mother and baby were discharged well on the 16th day of the puerperium.

An X-ray report of the lungs on 26th November, 1956 reads: "There has apparently been some incident at some time at the right base . . . probably was of the nature of a segmental collapse now recovering . . . and embolism is the commonest cause of this sort of picture."

A re-X-ray report on the lungs on 18th January, 1957 reads: "Appearances have now returned to normal and the lung fields are clear."

Discussion

Defective blood coagulation due to a haemophilia-like phenomenon in concealed accidental haemorrhage was described by DeLee as long ago as 1901 and in 1936 Dieckmann suggested that the bleeding was due to a marked deficiency in blood fibrinogen. Since that time numerous papers and reports on obstetric haemorrhage due to lowered blood fibrinogen have appeared.

Afibrinogenaemia or fibrinogenopenia is now recognized as occurring in association with cases of:

(1) Concealed accidental haemorrhage (Abruptio placentae).
(2) Some cases of prolonged retention of a dead foetus.
(3) Amniotic fluid embolism.

and may also occur in cases of:

(4) Eclampsia.
(5) Hydatidiform mole.
(6) Abortion.
(7) Severe haemorrhage as a secondary phenomenon.

Causation of Afibrinogenaemia

The most widely accepted theory of the cause of the lowered blood fibrinogen is that it is the result of widespread intravascular coagulation with resultant deposition of fibrin throughout the vascular bed and consequent depletion of blood fibrinogen. Schneider (1954) and also Weiner, Reid and Roby (1953) of Boston have developed the theory that the process is initiated by the release of tissue thromboplastins into the maternal circulation. It is suggested that damaged placental tissue and decidua are the source of thromboplastin which is expressed into the maternal circulation and it has also been shown that amniotic fluid contains appreciable quantities of thromboplastin. To some extent this theory is borne out by animal experiments.

With regard to the importance of afibrinogenaemia as a cause of haemorrhage in obstetrics, efficient uterine contraction and retraction is the normal means of averting haemorrhage after delivery. In the presence of afibrinogenaemia when haemorrhage begins it is likely to be severe and continuous; although if uterine haemostasis is good at delivery excessive loss need not occur even with very low blood fibrinogen levels (Jennison and Walker, 1956).

Amniotic Fluid Embolism

In this case I think the fibrinogenopenia was probably due to amniotic fluid embolism. Since this condition was first described by Steiner and Lushbaugh in 1941 as a cause of obstetric catastrophe, numerous papers have appeared with case reports. The typical syndrome appears to be sudden collapse with cyanosis during vigorous labour and anoxic convulsions may occur. Death commonly takes place quickly and at post-mortem examination amniotic debris is found in the pulmonary vessels.

The lethal factor in amniotic embolism has been uncertain—whether due to mechanical blockage or an anaphylactic reaction to the foreign protein; and even its reality as a cause of obstetric death has been doubted by some. However, there now seems to be quite a large number of well documented case reports in which amniotic pulmonary emboli together with incoagulable blood were the only significant post-mortem findings in cases of sudden death in obstetrics (Shotton and Taylor, 1949; Denniss *et al.*, 1954).

If the patient should survive the immediate episode, a lowered blood fibrinogen level with liability to profuse haemorrhage at delivery will develop. This concept of sub-lethal cases of amniotic embolism with subsequent afibrinogenaemia and severe post-partum haemorrhage was first offered by Reid, Weiner and Roby (1953). They reported five cases of collapse and cyanosis in labour with subsequent severe post-partum haemorrhage and low blood fibrinogen levels. Four of these cases recovered with blood transfusion and fibrinogen administration.

They consider that the term amniotic fluid infusion is preferable to amniotic fluid embolism and that the thromboplastin content of the amniotic fluid is sufficient to cause intravascular clotting and defibrination. However, demonstrable fibrin occlusions like those found in cases of abruptio placentae are rarely found in amniotic embolism and many workers consider that the incoagulable nature of the blood may be due to inhibition of coagulation by the

formation of antithrombins or a fibrinogenolysin as a secondary phenomenon.

In the case just described I think that amniotic fluid embolism is the most likely explanation of the sequence of events, although of course when the patient recovers the diagnosis cannot be confirmed. I feel that the alternative diagnosis of eclampsia is less likely in this case. There was no antecedent toxaemia, there was no definite fit, the blood pressure was low rather than high, the patient was collapsed and cyanosed at the commencement of the attack and there was no residual toxaemia.

Summary

(1) A case of severe post-partum haemorrhage with afibrinogenaemia following an episode of collapse and cyanosis before delivery is described.

(2) The case was successfully treated with administration of fibrinogen in the form of concentrated plasma and blood transfusion.

(3) The known causes of afibrinogenaemia and the likelihood of post-partum haemorrhage in cases of amniotic fluid embolism which survive is briefly discussed.

(4) It is suggested that amniotic fluid embolism was the probable cause of the afibrinogenaemia in this case.

I would like to thank Dr. K. V. Bailey, under whose care the patient was admitted, for permission to publish the case and for his help in the management, and Dr. Bailey and Professor Morris for their help in the preparation of this paper.

My thanks are also due to Dr. R. F. Jennison, Pathologist, for the fibrinogen estimations.

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THE PREVENTION OF CONGENITAL ANOMALIES IN THE HUMAN: EXPERIENCES WITH ALPHA TOCOPHEROL AS A PROPHYLACTIC MEASURE*

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INTRODUCTION

MUCH has been written on the causation of congenital anomaly. Until recently the emphasis in such discussions has been on genetic, mechanical, roentgenological, chemical, endocrine and infectious factors (Potter, 1952). But of late a great deal of experimentation has emphasized the role of nutritional factors. Indeed, Macy and Mack (1954) point out that deficiency of any one of some 13 nutrients has been blamed for the subsequent appearance of anomalies. Among those they named were vitamins A, E, C, B_2, B_{12}, pantothenic acid, folic acid, biotin, niacin, tryptophane, iodine, manganese and copper. This statement can be readily corroborated by reference to Warkany's fine review (1947), to a previous review by the writer (Shute, 1953a), and to recent papers on deficiency of pteroylglutamic acid (Monie, Nelson and Evans, 1954), vitamin A (*Nutrition Reviews*, 1954), riboflavin and B_{12} (Grainger, O'Dell and Hagan, 1954), pantothenic acid (Lefebvres, 1954), folic acid (Giroud *et al.*, 1954) or even excess of vitamin A (Cohlan, 1954).

It is now clear that congenital anomalies can originate before fertilization, as in Stockard's studies (1921) on sea minnows. Or they can develop just prior to organogenesis, as in X-irradiation experiments, or during organogenesis—as so well demonstrated by Warkany and many of the recent workers mentioned above. Moreover many of the defects produced by genetic factors can be duplicated by nutritional deficiencies, making what is called "phenocopies". An inherited tendency, as in the rabbit species tending to develop diaphragmatic hernias, may be accentuated by deficiency of vitamin A (Anderson, 1949).

Ingalls, Curley and Prindle (1952) have summarized the problem very well, after reporting their own studies on inducing anomalies in mice by suitably timed anoxia. They pointed out that folic acid, pantothenic acid, nitrogen mustard, vitamin B_{12}, trypan blue, methane, cortisone or artificial shock have all been implicated in experimental teratogenesis and conclude: "From the welter of investigations has come an ever-growing list of teratogenic agents. As the list grows steadily larger one is reminded of Conklin's enumeration of stimuli capable of causing artificial parthenogenesis—mechanical, chemical, thermal, electrical, and radiant. They include light, density of medium, gravity, and centrifugal force; oxygen, carbonic acid, water, food, secretions of ductless glands; salts, acids, alkalis, alcohol, ether and tobacco. The number of teratogenic agents is not yet as large as the number of parthenogenetic substances—or carcinogens, of which some 400 hydrocarbons alone have been identified. As the number rises, however, the question of specificity seems to become less important than dosage and timing of the agent used. The very diversity of teratogenic stresses and agents suggests that any substance that can kill can induce abnormal growth when acting in critical dosage at an appropriate moment of development. If this is so, then one of the important problems that confronts laboratory investigators is to study some agents quantitatively as well as qualitatively; measuring time when administered as well as dosage of agent;

* As read at the Second International Congress on Fertility and Sterility, Naples, Italy, May, 1956.

and measuring effects not only in terms of embryonic malformations but also in terms of embryonic mortality."

The evidence in man is much more vague than that provided by animal experiment, however. Studies on series of undernourished mothers, such as those summarized by McGanity *et al.* (1954), have not indicated an increased incidence of anomalies. Carter and Tizard (1954) believe that there is "no good evidence that malnutrition causes deformity in man". Potter shares this view, although quoting the observation that high protein diets can be preventive and noting the increased incidence of anomalies in the children of diabetic mothers. Gesenius (1951) reports that there was an increase of anomalous births in Germany after the second World War and mentions that a similar observation was made by Clesius in 1812, Breytag after the Thirty Years War, and by Legrand in 1871. Perhaps this was ascribable to maternal malnutrition, he suggests. We might add that Thoma recorded that, in the zoos of London and Berlin, tigers, lions and jaguars gave birth to cubs with hare-lip and cleft palate if the mothers were low in vitamins—and when the defect in diet was corrected, the litters became normal again (Kiskadden, Schecktman and Brock, 1949).

Still less has been done upon the relation between sperm morphology and the incidence of anomalies. The writer has found but one reference to this problem. Hinglais and Hinglais (1953) found that sires with defective sperms produced 3·4 per cent of anomalous children whereas men with normal sperms produced none. The writer has adduced evidence (Shute, 1953b, c) to indicate that sires who produced anomalies were less apt to do so if given alpha tocopherol before subsequent conceptions by the same mothers.

Much more could be said on this problem, but enough has been indicated in the references cited to show that maternal and probably paternal nutrition can influence the production of congenital anomalies among the offspring of experimental animals of many species, and perhaps of man.

Data

For 23 years the writer has practised obstetrics in an area where congenital anomalies appear to be relatively common (Shute, 1953c). That such areas exist on this continent was long ago demonstrated by Peterson (1934). During that time the author has cared for some 3,500 pregnancies. He has kept careful records on all the families having anomalies that he has encountered. This represents 336 pregnancies occurring in 104 families. Of these 146 produced normal children, 63 abortions or miscarriages, and 127 anomalies. It appears that initial sterility in the mothers, maternal age, the abortion rate, the rate of threatened abortion, birth rank, month of conception and consanguinity had no significant bearing on the origin of monsters in his series. However, some factors developed significance and are worthy of some separate consideration here:

Abortion Sequences

Abortions among siblings	40
Abortions adjacent to anomalous births	29
Abortions in both adjacent birth ranks	3
No abortions (where other births known)	58

Thus it would seem that abortions are frequent in families producing anomalies and often rank adjacent to the latter.

Sperm Studies

We have always found it difficult to persuade men that they could be involved in this problem. Hence we have secured sperm analyses on only 32 sires, although these analyses were often multiple when they were obtained. Seventeen of the 32 were grossly abnormal. A major defect seems to be poor motility (Bergman, 1955).

Heredity

Heredity was an obvious aetiological consideration in a few of these family histories. We have data on 94 families, and of these 94 there were anomalies in the adjacent branches of the family tree in 22. In 15 of the 22 they were very similar, and sometimes multiple. The inherited taint came through the male line 11 times, through the female line 11 times, and through both 4 times. By the laws of chance one would expect the parents to be equally responsible. However, as will be seen below, treatment directed at the male would suggest that the sire

was the more important of the two as a causative factor in the phenomena of anomaly.

Sex

Sex played a role in the incidence of certain types of congenital anomaly, at least.

Genito-urinary—10 males to 1 female.

Hare-lip and/or cleft palate—8 males to 4 females.

Viscera—10 males to 8 females.

Nervous system—30 males to 24 females.

Mongolism—3 males to 3 females.

Extremities and skeleton—17 males to 18 females.

The predominance of males in our series continues to be evident. Others (Murphy, 1937) have found differently, in certain types of anomalies at least.

The Repetition of Anomalies

Anomalies may repeat in siblings, although out of apprehension there is a natural tendency to restrict the size of such families voluntarily. Such a repetition occurred 19 times in our small series. These sequences appeared:

(1) Clubfeet with renal aplasia→Clubfeet and lung collapse.
(2) Meningocoele→Spina bifida and clubfeet.
(3) Defective hands→Spasticity.
(4) Spina bifida and meningocoele→Spina bifida.
(5) Clubfeet→Hare-lip.
(6) Spina bifida→Myelomeningocoele.
(7) Anencephaly→Meningocoele→Hydrocephaly.
(8) Hammer toes→Hammer toes.
(9) Meningocoele and hydrocephaly→Asymmetry of legs.
(10) Web toes and missing fingers→Congenital heart→Splenomegaly.
(11) Congenital heart→Mongolism.
(12) Hare-lip and meningocoele→Anencephaly →Hypospadias.
(13) Hare-lip and cleft palate→Anencephaly.
(14) Bowel atresia, mongolism and clubfeet→ Mongolism and clubfeet.
(15) Hare-lip and cleft palate→Hernia at fourth week of life.
(16) Clubfeet and deformed hand and eyes and congenital heart→Hydatid mole.
(17) Pyloric stenosis→Pseudohermaphroditism.
(18) Spina bifida→Spina bifida.
(19) Syndactyly → Syndactyly → Syndactyly→ Ear anomalies.

Murphy (1936) has estimated that the chance of a defective sibling appearing in a family already having one defective is increased 24 times. Of our 104 families 87 had 2 or more children. Among these there were 24 anomalies produced subsequent to the index monster, as well as 137 normal children. This indicates an expectancy of abnormal sibs where there has already been one defective of $\frac{24}{137+24}=1$ in 7. If the expectancy of anomalies amongst the general population in our locality is faithfully represented in my own private practice, it is $\frac{127}{3,500}=1$ in 28. Thus we conclude that in our locality the occurrence of one anomaly increases the likelihood of a second anomalous sibling appearing subsequently by 4 times.

The Effect of Giving Alpha Tocopherol to the Sire Prior to Conception

Failures. (The "controlled" pregnancy is indicated by italics.)

5226—Abortion→Normal→Meningocoele→ *Spina bifida.* (N.B.: The patient's aunt had a spina bifida.)

6600—Abortion→Abortion→Abortion→*Spina bifida and anencephaly.* (The mother and a maternal aunt had spina bifida.)

Successes. (The "controlled" pregnancy is indicated by italics.)

4813—Normal→Spina bifida and meningocoele →Spina bifida→*Normal.*

2075—Miscarriage→Turricephalic idiot→*Normal*→Normal. (N.B.: The patient's brother and nephew had asymmetry of the arms and legs. Her nephew was a spastic idiot.)

1631—Spina bifida and anencephaly and omphalocoele→*Normal.*

1588—Abortion→Hare-lip→*Normal.*

1531—Spina bifida and hydrocephaly→*Normal* →Miscarriage→Myelomeningocoele.

2662—Spina bifida and hydrocephaly→*Normal.*

2443—Normal→Bowel atresia and clubfoot and mongolism→*Normal*→Mongolism with clubfoot.

136—Webbed hands→Abortion→Abortion→*Normal.*

2941—Extracardia→Miscarriage→Abortion→*Normal.*

1157—Abortion→Spina bifida and anencephaly→*Normal*→Normal→Normal.

5339—Normal→Atresia of trachea→*Normal.*

4438—Normal→Atresia of trachea and dextrocardia→*Normal.*

3054—Anencephaly→*Normal.*

5528—Myelomeningocoele→*Normal.*

7491—Hydrocephalic→Normal→*Normal.**

It would seem that the result achieved was particularly happy in such cases as 4813, 1531, 2443, where there were two other abnormal sibs, as well as in cases 2075, 1631, 1588, 1531, 2662, 136, 2941, 1157, 3054 and 5528, where there had been no successful pregnancies before. Perhaps case 1531 is the most instructive, for there the treated pregnancy was the only success of 4 pregnancies. Professor Randal Cole has kindly analyzed these data statistically for me. He states:

"The 104 families under consideration contributed 336 pregnancies, of which 146 produced normal, 63 resulted in abortions or miscarriages, 127 resulted in monsters. The 17 'controlled' pregnancies produced 15 normal children and 2 anomalous infants.

"In order to assess the significance of this result, we may divide the 336 pregnancies into two categories. The 146 pregnancies which resulted in normal offspring will be called successful ones, and the remaining 190 will be called unsuccessful. If then we hypothesize that the treatment administered in the controlled pregnancies had no influence on the outcomes, we must attribute the results to chance alone or to a skilful selection of the recipients of the treatment. If a random selection of 17 pregnancies is made from the complete set of 336, the probability of obtaining 15 or more successful ones is ·000121. Since this is smaller than one chance in 8,000, and since the possibility of a skilful selection is not borne out by the histories of the families concerned, the hypothesis can be rejected with confidence.

"If we leave the 63 abortions and miscarriages out of consideration, the probabilities are still impressive. In this case the list includes 146 normal offspring and 127 monsters. The probability that a random selection of 17 from these will yield 15 or more normals is ·00213, or a little more than one chance in 500. It may also be of interest to note that the probability of getting 14 or more normals is ·0110."

Discussion

The study outlined above is a long-term investigation of personally observed patients in a geographic area where it appears that congenital anomalies are unusually common. It has taken the writer 23 years to accumulate these limited data, but such series are invaluable in a study of uncommon phenomena, and, indeed, at the moment, this one appears to have no parallel in medical literature.

It raises as many problems as it solves, perhaps.

Admittedly it deals only with the anomalies that are evident on gross inspection of the child. It was impossible for us to get routine post-mortems on all our dead babies, and unless such dead infants are *all* examined thus a large error is introduced. There may have been more anomalous children than we have discovered therefore, and more anomalies in those we did identify than we have recorded. However, the series is self-consistent, uses a standard criterion, viz., gross inspection, and errs on the side of conservatism where it errs. Any congenital anomalies missed in the so-called "normals" which have been born following tocopherol treatment have not been lethal, for all have survived in good health.

This study is based upon an assumption, namely that it is difficult to influence the integrity of the ovum (Juhasz-Schaffer, 1931; Evans, 1932; Bacharach *et al.*, 1937; Bergel,

* Through the courtesy of Dr. H. G. MacKichan of this city I can add another case (Mrs. G.R.) to this series. Her first two babies showed spina bifida and hydrocephalus. The husband took alpha tocopherol for four months prior to her next conception. The third child was normal at term delivery.

A recent patient of my own (Mrs. H.), has had an identical result by the same method. Her first two children had had anencephaly. The third was normal at term.

1939; Harris and Quaife, 1952; Carbonini, 1953; Evoli, 1954; Darlington and Chassels, 1956), but that alpha tocopherol can modify human sperm (Moench, 1936; Biskind and Falk, 1943; Shute, 1944, 1953c), at least qualitatively. What happens then if one attacks only the sire of anomalous children, and endeavours to improve his sperms before subsequent conceptions? Now the data in this study suggest that inherited taints are as common in the maternal as the paternal background of these families producing monsters. It is of interest, too, that the two failures recorded in the 17 trials occurred in families where the maternal taint was very obvious, was direct, and was identical in the two successive generations.

This study does not deny that inheritance plays a role in the causation of human anomalies. However, it does recall the work of Heston (1938) on bent-nosed rats. He was able to suppress this hereditary trait by giving adequate vitamin D or calcium and phosphorus to the tainted mothers. Perhaps alpha tocopherol is able to suppress hereditary taints in the sires of anomalous children. Whether such physically normal offspring as they then produce will carry the taint on to their own progeny will not be revealed for another generation. It is so likely, however, that it is to be hoped they will reproduce in a day when every sire will take alpha tocopherol before conception. Since we have never given it to the mother prior to conception we do not know what such an approach might have achieved. The recent study of Darlington and Chassels (1956) is especially suggestive in this regard. It may be that alpha tocopherol can qualitatively improve ova as well as sperms.

It is of interest that Shute (1936), Barrie (1937), as well as Cheng and Thomas (1953) have described congenital anomalies developing in the litters of vitamin E-deficient mother rats, and Ferguson, Atkinson and Couch (1954) in the progeny of vitamin E-deficient turkeys.

The implications of this study are of great importance, and deserve to be pursued by other investigators. No more hopeless or poignant situation confronts parents or obstetricians than the delivery of an anomalous child. What are the future prospects in that family? Our data indicate that, in our area at least, those prospects are very discouraging unless alpha tocopherol is utilized as suggested above.

Summary

(1) In a study of 104 families where grossly anomalous infants were born, 336 pregnancies produced 146 normal children, 63 abortions and miscarriages, and 127 monsters.

(2) In 17 of them the sire was given alpha tocopherol immediately prior to the conception of one or more pregnancies subsequent to the defective infant.

(3) In 15 of the 17 "controlled pregnancies" normal infants were produced. The probability of this occurring by chance is less than 1 in 500.

(4) In 4 such families there were children born to the same parents subsequent to the "controlled pregnancies", but in these instances the sire did not take alpha tocopherol before they were conceived. In 2 of the 4 such subsequent children were anomalous again.

(5) It is suggested that giving alpha tocopherol to the sire before any conception makes the subsequent birth of a normal infant more likely.

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MACROCYTIC ANAEMIA OF PREGNANCY

BY

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MACROCYTIC anaemia is usually considered as a rare complication of pregnancy but, when present, is an important cause of maternal morbidity. It occurs more frequently during pregnancy in tropical countries; nutritional deficiency appears to be a factor and a pointer to the aetiology of the condition in non-tropical countries, as will be considered later.

Numerous studies on macrocytic anaemias occurring in India have been made and publications include those of Wills and Evans (1938), Wills (1934) and Das Gupta, Chatterjea and Basu (1953). Reports from Africa include those of Adams and Wilmot (1953), Cohen (1953) and Berry (1955).

European publications have also stressed the importance, although comparative rarity, of the condition, which has such a wide geographical incidence.

The disease appears to occur more frequently amongst the poorer classes, possibly associated with dietary deficiency. The onset is usually insidious and occurs most commonly within the last three months of pregnancy.

A widely differing case incidence has been reported by various authors; Davidson, Davis and Innes (1942) give the incidence as 2 in 1,000 pregnancies and Moore, Lillie and Gatenby (1955) found 15 cases in 1,044 pregnancies. In this present small series, we were surprised to find 5 cases in a period of six months in our comparatively small obstetric unit, which deals with some 650 deliveries annually. The incidence will, of course, depend on several factors, including specific local factors (such as nutritional deficiency in India) and the figures will vary with the degree of observation and the availability of laboratory facilities; we would stress that a routine scheme should be adopted during antenatal surveillance, when economic consideration will permit of this; it is essential to obtain an early diagnosis and to differentiate from iron-deficiency anaemia, so that satisfactory therapy is instituted as early as possible.

CASE HISTORIES

Case 1 was a gravida-2, aged 33 years. She attended for the first time at the antenatal clinic when 27-weeks pregnant. There was no relevant previous history and, apart from some pallor, no abnormality was found on examination. Her haemoglobin was 52 per cent (7·7 g. per cent) and she was admitted to hospital for investigation and treatment.

Blood count on admission showed a haemoglobin level of 49 per cent (7·3 g. per cent); red cell count 3,660,000 per c.mm.; colour index 0·67; white cell count 9,300 per c.mm., with a normal differential count; the red cells showed marked anisocytosis, poikilocytosis and hypochromia.

The case appeared to be one of iron-deficiency anaemia and the patient was given intravenous iron to a total dosage of 1,800 mg. Little response was noted, a further blood count showing the haemoglobin to be 58 per cent (8·6 g. per cent); red cell count 4,450,000 per c.mm.; colour index 0·65; the red cells showed marked anisocytosis, poikilocytosis and anisochromia with moderate polychromia. Some macrocytic cells were seen in the film and it was thought that the anaemia resulted from a combined iron and haemopoietic factor deficiency.

Permission for marrow puncture and gastric analysis being refused, it was decided to treat the patient with vitamin B_{12}, 100 microgrammes weekly, and to follow her progress, which may be seen from the accompanying chart (Fig. 1).

HAEMOGLOBIN (g%)
HAEMOGLOBIN (g%)

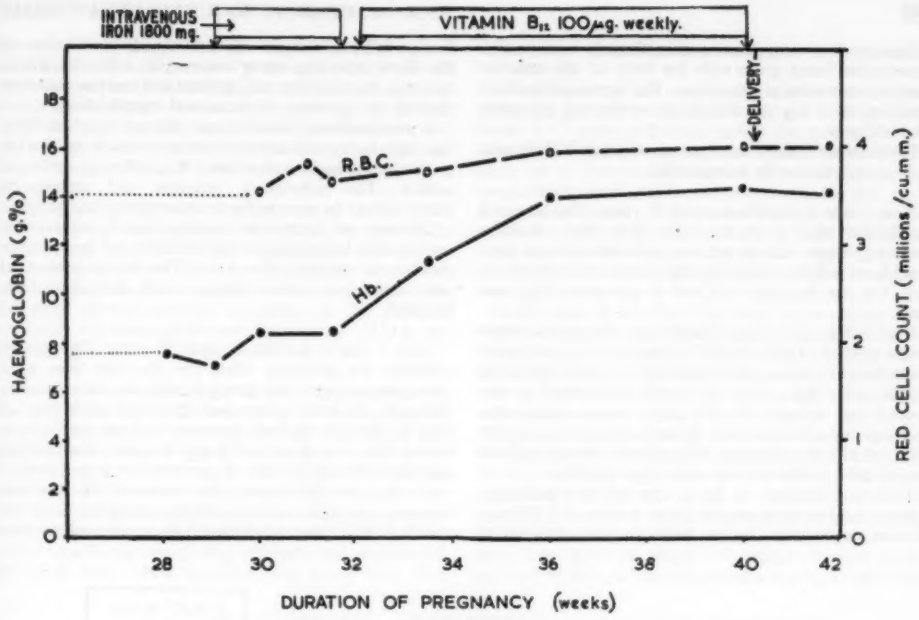

FIG. 1. Case 1

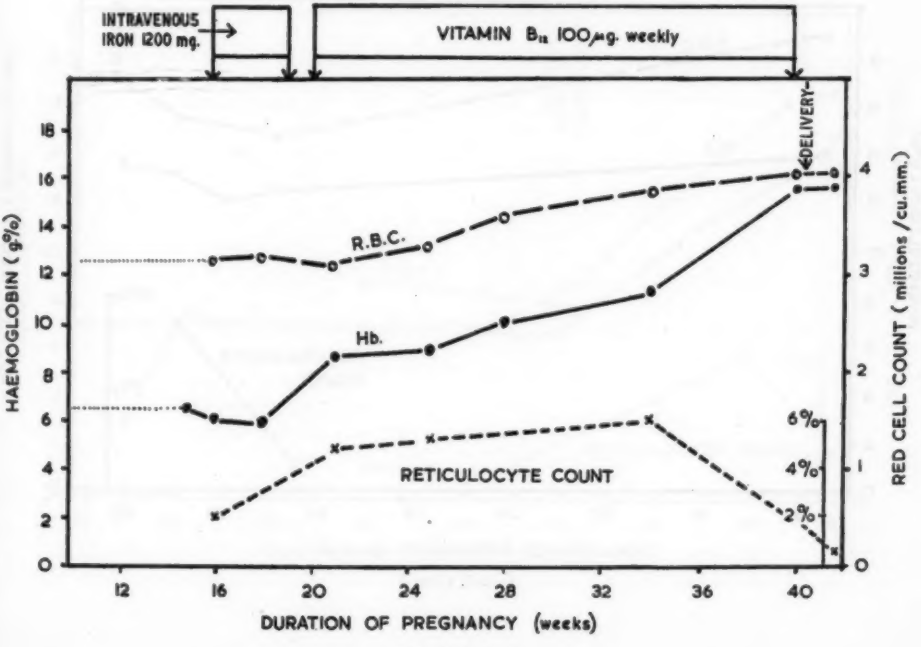

FIG. 2. Case 2

Delivery at term was uncomplicated, intravenous ergometrine being given with the birth of the anterior shoulder to minimize blood loss. The haemoglobin level remained at 13·7 g. per cent at two weeks and six weeks after delivery.

Reticulocyte counts were not carried out in this case, as it was the first to be encountered.

Case 2 was a gravida-2, aged 29 years. She attended for the first time at the antenatal clinic when 14-weeks pregnant. There was no relevant previous history and, apart from pallor, no abnormality was found on examination. The haemoglobin level was 45 per cent (6·7 g. per cent).

Blood count at the time of admission showed a haemoglobin level of 42 per cent (6·2 g. per cent); red cell count 3,190,000 per c.mm.; colour index 0·65; white cell count 10,800 per c.mm., with a normal differential count; packed cell volume 21 per cent; mean corpuscular haemoglobin concentration 30 per cent; mean corpuscular volume 66 c.microns. The red cells showed marked anisocytosis, poikilocytosis and hypochromia.

This was thought to be a case of iron-deficiency anaemia and the patient was given a total of 1,200 mg. of intravenous iron. As no response was obtained, a further full blood count was performed, examination of the films revealing many macrocytic cells. Histamine test meal revealed free acid present and marrow puncture showed the presence of occasional megaloblasts.

It was concluded that the case was one in which there was both iron and haemopoietic factor deficiency and the patient was treated with vitamin B_{12}, 100 microgrammes weekly. The subsequent progress and reticulocyte response may be seen on the accompanying chart (Fig. 2).

Delivery at term was uncomplicated, intravenous ergometrine being given with the birth of the anterior shoulder to minimize blood loss. The haemoglobin level was maintained after delivery and discharge from hospital.

Case 3 was a gravida-2, aged 23 years. The patient attended the antenatal clinic for the first time when 12-weeks pregnant, She gave a history of severe anaemia following the birth of her first child, for which she had been transfused. Marrow puncture had been carried out at that time. No abnormality was found on examination and her haemoglobin was 98 per cent (14 g. per cent).

In view of the history, the slides of the previous marrow puncture were examined, together with the report at that time, which stated that megaloblasts were

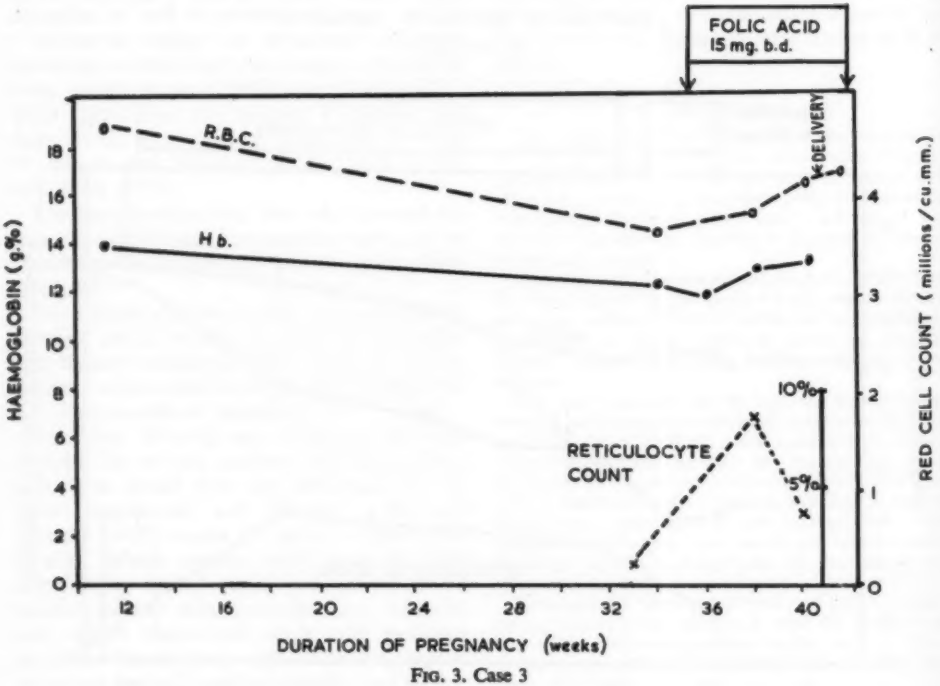

FIG. 3. Case 3

present. It was thought that this might well have been a case of macrocytic anaemia of pregnancy and the patient was observed carefully during pregnancy, regular blood counts and haemoglobin estimations being carried out.

The red cell fragility was within normal limits, the direct Coombs test was negative and the serum bilirubin level 1·5 mg. per cent. Histamine test meal revealed free acid present.

At the thirty-fifth week of pregnancy, there was a fall in the haemoglobin level and the patient was given folic acid, 15 mg. twice daily. Her response is shown on the accompanying chart (Fig. 3). Delivery at term was uneventful, intravenous ergometrine being given with the birth of the anterior shoulder. At the time of discharge, the haemoglobin was 94 per cent (13·6 g. per cent).

Case 4 was a gravida-2, aged 32 years. She attended the antenatal clinic for the first time when 26-weeks pregnant. Apart from pallor, no abnormality was found on examination, but she gave a history of attacks of diarrhoea and vomiting as a child and of subsequent attacks of diarrhoea since that time. She stated that she had been under investigation for anaemia at one time, but that she was on no specific treatment. Her haemoglobin was 50 per cent (7·0 g. per cent) and remained at the same level when repeated four weeks later. She was advised admission for investigation and treatment, but refused.

A full blood picture was carried out, however, which showed a red cell count of 2,300,000 per c.mm.; colour index 1·1; white cell count 6,400 per c.mm., with a normal differential count; packed cell volume 21 per cent; mean corpuscular volume 91 c.microns; mean corpuscular haemoglobin concentration 30 per cent; reticulocyte count 1·8 per cent. The red cells showed marked anisocytosis, poikilocytosis, polychromasia and moderate hypochromia and basophilic stippling. It was concluded that these findings were compatible with a macrocytic anaemia.

In the interval between this blood count and her next clinic attendance, the patient had been given 800 mg. of intravenous iron by her own doctor. At this clinic attendance, she was again advised admission for marrow puncture and histamine test meal, but again refused. She was therefore treated as an out-patient with vitamin B_{12}, 100 microgrammes weekly, for three weeks. Further blood examination then showed the haemoglobin to be 47 per cent (7·0 g. per cent); red cell count 1,970,000 per c.mm. and a reticulocyte count of 1 per cent. In view of the lack of response and the lateness of the pregnancy, the patient was persuaded to enter hospital. She was given two pints of Group A, rhesus positive cross-matched blood and was also given folic acid, 15 mg. twice

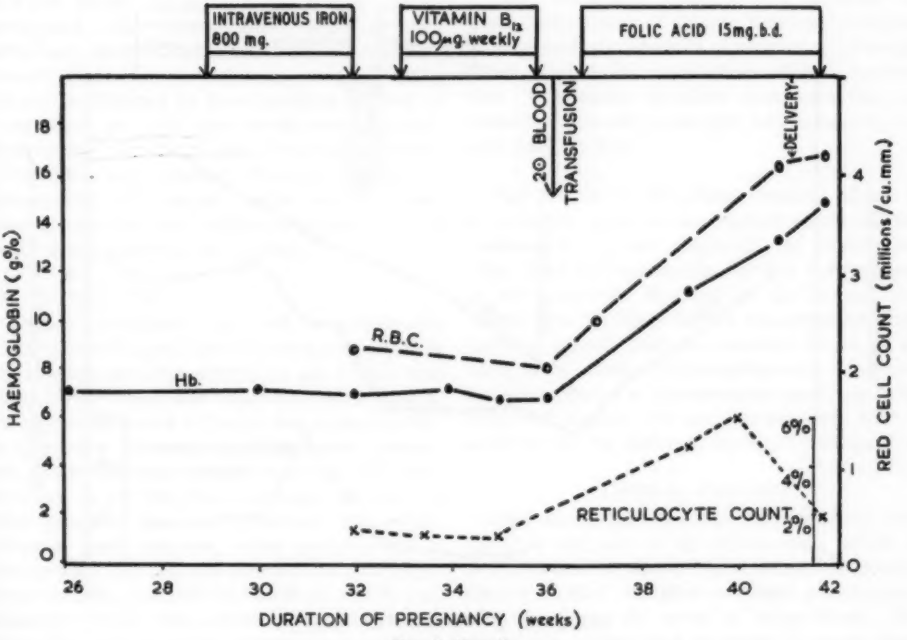

FIG. 4. Case 4

daily. Her progress and the reticulocyte response are shown on the accompanying chart (Fig. 4).

Delivery at term was uneventful. Two weeks after delivery, the haemoglobin level was 90 per cent (13·3 g. per cent); red cell count 4,110,000 per c.mm. and the reticulocyte count 1·8 per cent.

There was a strong suspicion that the basis of the macrocytic anaemia in this case was an idiopathic steatorrhoea and it is unfortunate that permission was not obtained for complete investigation.

Case 5 was a gravida-3, aged 26 years. She attended the antenatal clinic when 22-weeks pregnant. No abnormality was found on examination and the haemoglobin was 78 per cent (11 g. per cent). She attended regularly until the thirty-second week of pregnancy, not being seen again until the thirty-eighth week. She stated that she had been under treatment during this time for sore throats and had been given sulphonamides by her doctor, with little improvement. Examination revealed her to be pale and unwell and the haemoglobin was 35 per cent (5·2 g. per cent). She was admitted to hospital.

The red cell count was 1,740,000 per c.mm.; colour index 1·0; white cell count 3,600 per c.mm., with a normal differential count. Nucleated red cells were seen in the peripheral film, some of the cells being undoubted megaloblasts. Histamine test meal revealed free acid present.

It was concluded that this was a case of macrocytic anaemia of pregnancy.

In view of the nearness of the expected date of delivery, the patient was transfused with two pints of Group O, rhesus positive, cross-matched blood.

She went into labour the following day and had an uneventful delivery, intravenous ergometrine being given with the birth of the anterior shoulder in order to minimize the blood loss.

After delivery, the patient became febrile and remained so for 11 days. All investigations were negative and it was thought that the temperature was associated with the macrocytic anaemia. However, in view of the low haemoglobin level, she was given prophylactic penicillin, 1,000,000 units daily.

She was given vitamin B_{12}, 100 microgrammes, after delivery and her response over the succeeding seven days noted. The maximum reticulocyte count was 1·5 per cent and, as her haemoglobin level remained at 45 per cent (6·5 g. per cent), she was given a further pint of blood and treatment was commenced with folic acid, 15 mg., twice daily. Her response and the reticulocyte count are shown on the chart (Fig. 5). Six weeks after delivery, the haemoglobin level was 92 per cent (13 g. per cent) and the red cell count 4,250,000 per c.mm.

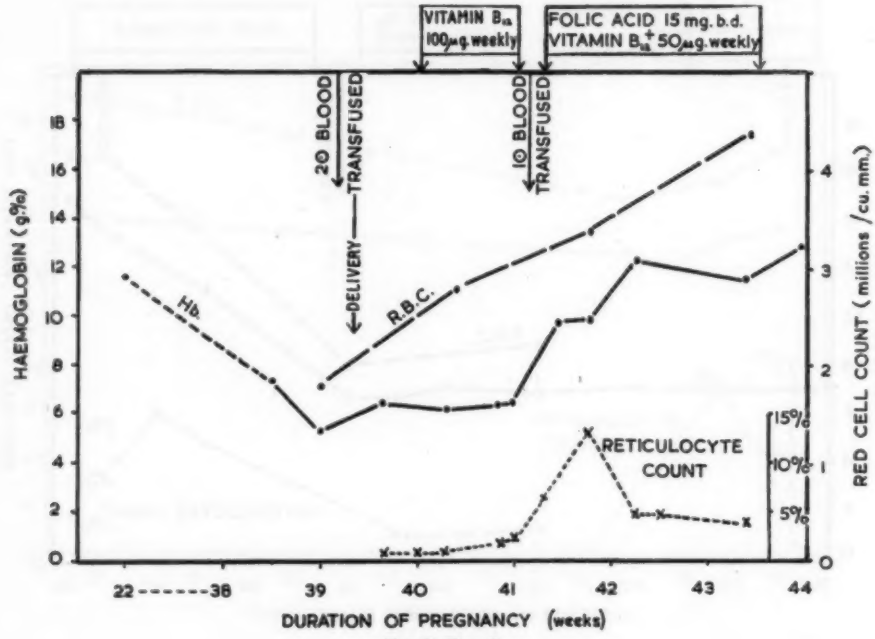

FIG 5. Case 5

This patient has been seen successfully through a subsequent pregnancy, being given folic acid, 15 mg. daily and vitamin B_{12}, 100 microgrammes weekly, throughout the pregnancy.

Aetiology

Two main varieties of macrocytic anaemia may be encountered in pregnancy. In the first, the condition is independent of, though associated with, pregnancy and here are included cases of Addisonian anaemia, diagnosed prior to or during pregnancy, and cases of tropical nutritional macrocytic anaemia.

The second variety comprises those cases of macrocytic anaemia occurring in, and due to, pregnancy and it is with this latter group that we are here concerned. Possible aetiological factors have been suggested and these are now outlined:

(a) *Temporary Intrinsic Factor Deficiency*

The known depression of gastric secretion during pregnancy suggests that there might be a corresponding reduction in the secretion of intrinsic factor. Thompson and Ungley (1951) concluded, after investigation, that no such deficiency existed and pointed out further that, should there be such deficiency, a good result should be obtained by liver injection. In fact, in their cases, no such good result was obtained. Badenoch, Callender, Evans, Turnbull and Witts (1955) have been unable to find any evidence of abnormality of intrinsic factor secretion and have shown a normal uptake of vitamin B_{12}, the latter being labelled with cobalt ^{60}.

(b) *Defective Diet*

Dietary deficiency may well constitute the essential aetiological factor in tropical countries and papers by Das Gupta *et al.* (1953) and Berry (1955) emphasize this point. Nevertheless, the degree to which defective diet is responsible in temperate climates must, at present, remain *sub judice*. Thompson and Ungley (1951) drew attention to the fact that, although the diets of some patients who had developed macrocytic anaemia were deficient, other patients on a similar poor diet did not develop the condition. Other writers, namely, Nieweg *et al.* (1954) and Heinrich (1954) have drawn attention to low serum vitamin B_{12} levels in the condition and the favourable response which followed oral administration of the vitamin. It was therefore postulated that there might exist a state of hypovitaminosis B_{12}, due to an increased demand during pregnancy and lactation. Badenoch *et al.* (1955) found, however, no abnormality of the serum vitamin B_{12} levels in any of the cases that they investigated.

(c) *Defective Absorption*

It has been shown by fat balance studies that defective intestinal absorption is more common than is generally believed and it has been suggested that an occult steatorrhoea may be a contributing factor in the production of the macrocytic anaemias of pregnancy. Recently, Badenoch and co-workers (1955) found no abnormality of fat absorption in 6 out of 9 cases of macrocytic anaemia investigated by them, although they were unable to exclude steatorrhoea in one case.

(d) *Hormonal Theory*

Day, Hall and Pease (1949) reported an abnormal pattern of urinary hormone excretion in megaloblastic anaemia of pregnancy, although other workers have not been able to confirm this. It remains possible, however, that an abnormal steroid is present, which is antagonistic to folic acid.

Any or all of the above factors, added to a possible increase in requirements of the maturation factors required for foetal red cells, may be responsible for the development of the condition. Workers on the subject have stated that the ideas on the causation are fluid and are agreed that the common factor in all cases is the relationship to pregnancy. The cases do not represent a homogeneous group and this may well explain the variable response that is obtained to the different forms of treatment.

General Features

That macrocytic anaemia of pregnancy may occur at any age in the childbearing period is well known. The time of onset is most commonly during the last trimester or in the puerperium, although cases do occur at other times. The symptoms, which may be acute in some cases

and insidious in others, are those of anaemia with, possibly, gastro-intestinal upsets, sore tongue, jaundice and splenomegaly. In many cases, however, there are no symptoms and diagnosis results from routine haematological investigation.

Treatment

It has been shown that many cases of macrocytic anaemia of pregnancy are refractory to injections of liver extract, although they may respond to whole liver or crude extracts orally. With the introduction of vitamin B_{12} and folic acid, recent reports have been concerned with the use of these two substances in treatment, although no unanimity has been reached as to which of the two should be used in any given case. Adams and Wilmot (1953), reporting on the condition in African and Indian women, stated that they had obtained a response in some cases from the administration of vitamin B_{12}, in others from folic acid and in yet others from the simultaneous administration of the two drugs. Similar results were obtained by Cohen (1953) in the treatment of the condition in Bantu women.

Das Gupta *et al.* (1953) reported on the treatment of the condition in Indian women and stated that they had had a response in some 70 per cent of cases following parenteral vitamin B_{12}, but that the response was not sustained if therapy was continued. If either folic acid or crude liver extract was given to these patients, then the response was sustained and the authors concluded that their cases represented a combined deficiency of the two substances. Berry (1955), reporting from West Africa, treated 13 of his 30 cases with vitamin B_{12} and obtained a satisfactory response, but added that folic acid might be required in order to obtain complete remission of the anaemia. In his series, there were many cases complicated by liver disease and blood parasites.

Turning to reports from this country, Thompson and Ungley (1951) reported little response with parenteral liver extracts or vitamin B_{12}, but noted that folic acid was effective in association with iron therapy. Israels and Da Cunha (1952) treated all their cases satisfactorily with folic acid whereas Badenoch *et al.* (1955) reported some cases which responded to vitamin B_{12} and others which responded only to folic acid. The latter workers also pointed out that the deficiency may well be relative, in so far as remission does occur after delivery in cases which have received no treatment.

Present Series

Case 1. This case presented as an iron-deficiency anaemia and the true nature of the condition was discovered only after a course of intravenous iron had been without effect. There was a satisfactory response to vitamin B_{12}, 100 microgrammes weekly.

Case 2. This case was thought to be one of iron-deficiency anaemia and the true nature of the condition only discovered after ineffectual iron therapy. Treatment with vitamin B_{12} produced a satisfactory response.

Case 3. The history of a severe anaemia after the birth of her first child and examination of the marrow biopsy taken at that time led us to believe that she had had a macrocytic anaemia of pregnancy at that time. The fall in haemoglobin at the 35th week of pregnancy was treated by folic acid, 15 mg. twice daily, with a satisfactory response.

Case 4. Difficulties were encountered with this patient, but both iron therapy and vitamin B_{12} were of no value. Folic acid produced a good result, even though transfusion had been given.

Case 5. Treatment with vitamin B_{12} was minimal in this case, but the simultaneous administration of folic acid produced a good result, even though the patient had received a blood transfusion.

Of these cases, three were observed to have pallor without symptoms, the diagnosis resting on laboratory investigation; one was observed after diagnosis was established from her past history and present investigation and the last was diagnosed after routine haematological examination, although the history in this case suggested that there may have been steatorrhoea present. Only one of the cases gave a history of minor gastro-intestinal disturbance and in no case was there jaundice or splenomegaly. In common with other workers, we have noted the variable response to the two substances used,

the final choice being dependent on the response of the patient.

The inter-relationship between folic acid, vitamin B_{12}, ascorbic acid and folinic acid (or the citrovorum factor, which is probably the active form of folic acid) has been discussed by Davis and Brown (1953) and Ungley (1955). It is suggested that the formation of nucleic acid is dependent on a series of stages in which folic acid and vitamin B_{12} each play an essential part, possibly as part of enzyme systems, so that a deficiency of either may then be responsible for a breakdown in nucleic acid metabolism. It is known that patients with a deficiency of folic acid will respond to the citrovorum factor in addition to the former and it is interesting in this respect to note that Holly (1951) has obtained a response in a macrocytic anaemia, refractory to vitamin B_{12} alone, by using vitamin B_{12} together with ascorbic acid.

Discussion

Examination of blood films is necessary for the diagnosis of macrocytic anaemia, there being, in a typical case, macrocytes and possibly megaloblasts in the peripheral blood. Although this is the typical picture, reliance must not be placed entirely on the film, for macrocytes may be scanty or absent in atypical cases and the general impression may be that of iron deficiency anaemia. It has been emphasized that the possibility of a macrocytic anaemia should be considered in any case of severe anaemia in pregnancy and it is recommended that marrow puncture be carried out before instituting specific treatment, for the features required to confirm the diagnosis are the presence of megaloblasts in the peripheral blood and a megaloblastic marrow. Gastric analysis may reveal free acid present, but in all cases a histamine test meal should be used.

Therefore, before the diagnosis can be certainly made, a full blood examination must be performed, marrow puncture carried out and gastric secretion studied. In addition, differentiation from a case of true Addisonian anaemia may be made in some cases by microbiological assay of the serum vitamin B_{12} level.

Whilst such examination may be desirable, to ensure early and correct treatment of such anaemias, it must be remembered that the commonest form to be encountered in pregnancy is the simple iron-deficiency anaemia and to suggest that the above investigations should be carried out in all cases of anaemia encountered in pregnant women would be quite unjustified, both from economic considerations and from the amount of work entailed for the laboratory staff, particularly where the latter are busy with routine examinations.

Because it is desirable for early diagnosis to be made and appropriate treatment commenced, we have attempted to formulate a scheme of investigation and treatment which may aid in the selection of those cases which display a macrocytic anaemia and the following are the points raised:

(*a*) Estimation of the haemoglobin forms an integral part of the examination of all patients at the first antenatal attendance.

(*b*) Although some cases in our series showed a low haemoglobin level at the time of their first visit, others developed the anaemia considerably later on in pregnancy.

(*c*) Those cases showing anaemia at the first attendance should be treated with additional dietary iron and ascorbic acid or, should dietary iron not be tolerated, parenteral iron may be employed.

(*d*) All cases attending the antenatal clinic should have a further haemoglobin estimation carried out between the 32nd and 36th week of pregnancy.

(*e*) Any case not responding to additional iron and ascorbic acid or any case showing anaemia (haemoglobin of less than 10 g. per cent) in the latter weeks of pregnancy should be further investigated by the methods mentioned.

(*f*) Although the deficiency is commonly of folic acid, we have found, in common with other workers, that some cases respond well to vitamin B_{12} and treatment may therefore be with one or other of the drugs, depending on the response. In certain cases, the two may be used together.

(*g*) When interpreting the haemoglobin readings, some allowance should be made for the physiological haemodilution of pregnancy.

(*h*) As some cases present late and there may not be sufficient time for final diagnosis to be made, early investigation may be performed should a further pregnancy ensue.

Summary

A small series of cases of macrocytic anaemia of pregnancy occurring within a six-months period in an obstetric unit is described, together with a brief review of the condition.

Initial diagnosis in 4 cases was of an iron-deficiency anaemia and final diagnosis was reached only after failure of response to intravenous iron.

A scheme of investigation and treatment is suggested, whereby such cases may be separated from the more commonly occurring cases of iron-deficiency anaemia without overtaxing the facilities of a laboratory dealing primarily with routine investigations.

Acknowledgments

We would like to thank Mr. Humphrey Arthure for his permission to publish the case histories of the 5 patients in this series.

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CONGENITAL ICHTHYOSIS (HARLEQUIN FOETUS)

BY

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THE "Harlequin" foetus is the most severe form of congenital ichthyosis. The condition is very rare; most infants with this extreme form of disease are either stillborn or die soon after birth. The body is completely covered with thick, firm, abnormal skin in which marked fissuring may occur. Bilateral ectropions are frequently present in the severe cases, being due to the contraction of the abnormal skin. The ears may also be abnormal in formation and the aural orifices may be completely closed. Kebrer (1928) discussed the microscopic appearances of the skin which shows marked hyperkeratosis with many single anuclear horny cells present in aggregations; furthermore the sweat and sebaceous glands were decreased. Waring (1932) cited an early reference to this disease by Hart in 1750. Caffier (1929) recorded three cases of the disease occurring in a single family. Williamson (1934) and Lattuada and Parker (1951) reviewed the literature in relation to congenital ichthyosis and also recorded cases of the condition. Further cases were reported by Seitz (1936), and a milder type of ichthyosis with collodion skin due to lamellar ichthyosis was reported by Finlay and Bound (1952); in this case the collodion skin affected the dorsum of the hands, fingers, feet and toes and the condition improved with desquamation of the abnormal areas leaving normal skin underneath.

CASE REPORT

An apparently healthy mother aged 23 years gave birth to her second child prematurely as a breech presentation after a pregnancy of about 30 weeks. The mother had a slight haemorrhage early during this pregnancy.

Her first child was abnormal and stillborn, the abnormality being a similar one to this child. The Wassermann reaction of the mother was negative and she was Rh positive Group A. This child, a female, was small, with a weight of 3 pounds and measuring 16 inches in length. The skull circumference was 12 inches. Bilateral ectropions were present with the exposed conjunctivae of the upper lids reddened and swollen. The ears were completely encrusted with vernix-like material and were dry and caked. The external meatus of each ear was closed with whitish keratinized material. The skin of the face was encrusted with thick, dry material simulating pale vernix caseosa. The lips appeared reddened and dry, in sharp contrast to the abnormal skin of the face. The whole body was covered with thickened, hard, caked, dry, light-brownish skin with irregular cracks and fissures present over the whole area. The deep fissuring and cracking of the abnormal skin was most marked at the flexures of the extremities. The toes were small and underdeveloped and the skin of the feet was tense and swollen and bullous in some areas. The hands were stiffened and swollen, and the fingers were small and underdeveloped with flexion contractures (Fig. 1).

The cardiac rate was 100 per minute; there was no evidence of any cardiac abnormality. The respiratory system was normal and no abnormality was detected in the abdomen.

The child survived for 3½ days during which time she took feeds fairly well.

Autopsy confirmed the gross abnormalities of the skin. The eyes were normal and the heart, brain, thymus, thyroid, suprarenal, liver, spleen,

stomach and bowel were free of gross abnormality.

The kidneys on section showed gross congestion of the medulla with a very pale cortex suggestive of a lower nephron nephrosis (acute tubular necrosis) which was confirmed by histological examination. The lungs showed patchy atelectasis. The histological examination of the skin (Dr. W. J. Pepler) showed the features of ichthyosis congenita; these features were marked hyperkeratosis and follicular plugging. The stratum granulosum was still present, but very atrophic. The rete Malpighii was thinner than normal and the rete pegs were diminished in number; the remaining rete pegs were elongated and thin (Figs. 2 and 3).

Histological examination of the cardiac muscle, liver, eye, brain, suprarenal and thymus gland showed no significant pathological changes.

This case shows the typical features of the extreme form of congenital ichthyosis known as the "Harlequin" foetus. The mother had a previous abnormal stillborn infant suggestive also of a skin abnormality. In 1929 Caffier recorded 3 such cases born of one mother, suggesting a familial basis for the condition.

The presence of a lower nephron nephrosis in this child is interesting in relation to the rare occurrence of this condition in the newborn; it has been previously recorded by one of us (I.K.) in a newborn infant dying of severe anoxia.

Summary

A case of the severe form of congenital ichthyosis (Harlequin foetus) is reported with a photographic record of the child. The mother had previously had a stillborn child with the same condition. Autopsy also showed the presence of a lower nephron nephrosis (acute tubular necrosis).

The literature is briefly reviewed.

Addendum. The mother of the patient recorded in this paper has recently given birth to a normal child.

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FIG. 1

Photographic study of a "Harlequin" Foetus.

(From *The Essentials of Paediatrics for Nurses* by I. Kessel through the courtesy of Messrs. E. and S. Livingstone, Ltd.)

FIG. 2
Histological section of skin. ×32.

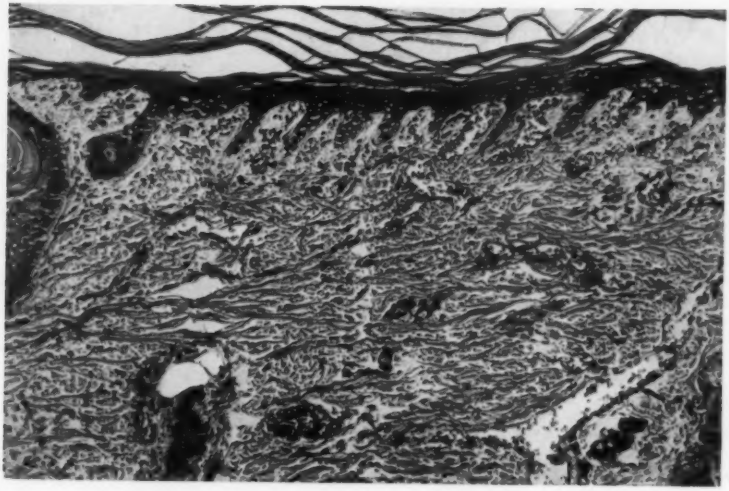

FIG. 3
Histological section of skin. ×120.

TRUE UNICORNATE UTERUS

Report of a Case with a Review of the Literature

BY

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ESTIMATES of the incidence of congenital anomalies of the female genital tract are subject to considerable variation. A. M. Campbell (1933) estimated that such abnormalities occur in one per cent of pregnancies and Moore (1941) found from his private records that 1 : 500–600 females had some deviation from the normal in their genital tracts. Taylor (1943) and Eisamen (1944), however, stated that partial or complete failure of fusion of the Müllerian ducts occurred in 1 : 15,000 obstetrical patients and 1 : 2,000 gynaecological patients. Moreover it would appear that the incidence of such abnormalities is influenced by the zeal of the investigator. Smith (1931), at the New York Lying-In Hospital, in investigating double uterus, personally found an incidence of 1 : 1,458 whereas in the previous 25 years it was recorded as 1 : 7,040. Some cases must pass unrecognized, others are chance findings at autopsy or laparotomy, or come to light as the cause of abnormal occurrence or difficulty in pregnancy and labour.

There is general agreement, however, that true unicornate uterus is the rarest of the congenital abnormalities of the female genital tract, especially when this anomaly is differentiated, as it should be, from unicornate uterus with a rudimentary horn, since they represent different developmental defects. The former condition is a result of complete or partial agenesis of a Müllerian duct while the latter arises from the failure of fusion of the lower ends of the ducts. The rarity of true unicornate uterus is shown by the experience of Pfleiderer (1929) who, in a review of the work of the Tübingen Frauenklinik over a period of 20 years, found 93 cases of genital abnormality but was unable to record a single case of unicornate uterus.

It was considered therefore that the following case was of sufficient interest and rarity to warrant reporting it.

CASE REPORT

Mrs. J.A., a primigravida, aged 25 years, was admitted to hospital on 29th November, 1951. Her L.M.P. had started on 21st July, 1951, giving the expected date of delivery 28th April, 1952. She complained that for about a month before admission her feet and ankles had been swollen and she had noticed puffiness of her face in the mornings. She had had no headache or vomiting. Micturition had been normal.

Examination showed a thin, pale, unco-operative young woman of below average intelligence. There was some puffiness of the upper eyelids and pitting oedema of both feet and ankles. No abnormality was found in heart or lungs. Her blood pressure was 140/80. The mucous membranes were of good colour. Abdominal examination showed the uterus enlarged to the size of a pregnancy of about 18-weeks duration and in addition a cystic swelling was palpable bimanually, extending downwards from the costal margin into the right loin. The urine was acid, of specific gravity 1006, and contained a heavy cloud of albumin (4 parts Esbach). Microscopically no casts or cells were seen. There was no growth on culture.

Examination of the blood gave the following results: Haemoglobin 80 per cent, red cells 4·05 million per c.mm., white cells 13,400 per c.mm. with 77 per cent polymorphs. The blood group was A Rh positive. The blood urea was 75 mg. per 100 ml. The total plasma proteins were 3·79 g. per 100 ml.—albumin 1·39 g. and globulin 2·4 g.

Intravenous pyelography was performed and the radiologist reported a marked hydronephrosis present on the right side. There was no secretion on the left side and no kidney shadow was visible. A foetus of 4 to 5 months gestation was seen.

A diagnosis of chronic nephritis was made and, especially in view of the fact that apparently only one kidney was functioning, termination of pregnancy and

sterilization were advised. The patient refused this advice on religious grounds.

Her general condition remained stationary until the end of December, 1951, when she was finally persuaded to submit to operation.

Laparotomy was performed through a lower right paramedian incision on 29th December, 1951, under gas, oxygen, trilene and ether anaesthesia. On opening the peritoneal cavity one was struck by the vascularity of the area of uterus which presented. A mass of dilated vessels was coursing across the uterus from its right side. The uterus was centralized with difficulty and hysterotomy was performed through a longitudinal incision in the upper segment. A female foetus 22 cm. in length was delivered. The uterus was closed with three layers of sutures. The right tube was sectioned, the proximal end buried in the uterus and the distal end peritonealized.

On turning to deal with the left tube, we found that the left iliac fossa was empty. Broad ligament, Fallopian tube, round ligament and ovary were absent. The left side of the uterus was free from attachment to the lateral wall of the pelvis. The peritoneum over the left side of the uterus merged with the peritoneum of the bladder at the vaginal vault and merged with the parietal peritoneum. No kidney was palpable on this side. The abdomen was closed in layers.

A diagnosis of true unicornate uterus with left renal agenesis was made.

In the early post-operative period there was some increase in the oedema and some congestion of both lung bases, but otherwise the patient made satisfactory progress and took her own discharge on 19th January, 1952.

No further trace of the patient was found until she was admitted to the medical wards of the hospital on 31st December, 1953 with a history of epistaxis and weakness of 2-weeks duration. Examination showed a very ill woman with puffiness of her face and ankles, blood pressure 180/100 and a dense cloud of albumin in her urine. Her heart was enlarged to the left and a pericardial rub was present. Her blood urea was now 300 mg. per cent and rose later to 700 mg. per cent. Her haemoglobin was 30 per cent, erythrocyte sedimentation rate 70 mm. in one hour (Wintrobe) and packed cell volume 15 per cent.

She was discharged unchanged on 14th January, 1954 and died at home in uraemia a few weeks later.

Review of the Literature

In the present review it has been possible to find mention of only 53 cases of true unicornate uterus in the available literature, including the case now reported. The only previous case reported in this country is that of Brackenbury (1891).

Six other cases are mentioned which might possibly have been included but the evidence is insufficient to classify them as cases of true unicornate uterus. M. F. Campbell (1928) reported the finding of a unicornate uterus in post-mortems on 2 young infants and Collins (1932) reported a similar finding, but neither author states whether the condition was a true unicornate uterus or was a unicornate uterus with a rudimentary horn. Jarcho (1946) also diagnosed 2 cases of unicornate uterus by hysterosalpingography but again the possibility of a rudimentary horn cannot be ruled out. Masson and Kaump (1937), in a review of 17 interesting anomalies of the female genital tract, record the post-mortem findings in a woman of 33 years. In this case the right tube, ovary, kidney, ureter and suprarenal gland were absent but no comment is made on the uterus itself.

Of the 53 cases mentioned above only one had been diagnosed clinically as a probable unicornate uterus. Tucker and Baker (1953) describe a primigravida of 28 years with several congenital anomalies which included congenital absence of one kidney, spina bifida occulta and marked asymmetry of the pelvis. From these associated abnormalities they assumed the presence of a unicornate uterus also. The diagnosis was confirmed at Caesarean section. Thirteen cases were diagnosed at laparotomy (Guthrie and Wilson, 1909; Dannreuther, 1923; Duncan, 1933; Schumaker, 1938; Cabanes and Jahier, 1938; Varino and Beacham, 1941; Whittemore, 1942; Jarcho, 1946; Alexander, 1947; Daro, Gollin and Nora, 1950; Taber, 1950; Ungerleider, 1952; Ogilvie, present case) performed in most cases for indications unconnected with the uterus itself. The remaining cases appear to have been found at autopsy.

Varying opinions have been expressed regarding the occurrence of pregnancy in true unicornate uterus. A. M. Campbell (1933) has stated that, in general, genital anomalies have a negligible effect on fertility; where there is a functioning ovary and a permeable Fallopian tube which connects with even a rudimentary uterus it is usually possible for fertilization and nidation to occur. Stander (1941) expresses the view that pregnancy in a unicornate uterus tends to be uneventful and this opinion is shared by DeLee and Greenhill (1947). Kussmaul (1859) also pointed out that pregnancy and delivery may occur. Munro Kerr and Chassar Moir

(1949), commenting on the rarity of this type of uterus, contend that the occurrence of pregnancy is even more so. Dannreuther (1923) considered the occurrence of pregnancy in his case unique.

Unfortunately the obstetric and menstrual histories of many of the recorded cases, especially those early in the series, are very incomplete. Of the reported cases 7 were infants or stillborn foetuses and in 19 other cases the details of age and obstetric history are lacking. The remaining 27 women were in or had passed through the reproductive period; of these 3 were unmarried and no obstetrical details were available in 7, but, of the remaining 17, 13 had been pregnant 35 times producing 28 infants and 7 abortions.

Assuming that all the patients for whom no details are available were in fact of reproductive age and had remained sterile, 13 in a total of 43 women with unicornate uterus, i.e., 30 per cent, had become pregnant. Thus at least 1 in 3 had become pregnant. It would seem therefore that pregnancy is not uncommon in unicornate uterus.

Schumaker (1938) has commented that in a number of cases spontaneous abortion occurs but it is impossible to state whether the uterine anomaly is responsible for this occurrence. Seven of the pregnancies recorded above ended in abortion. The case now reported had a therapeutic abortion, another (Alexander, 1947) had had a criminal abortion, while a third (Taber, 1950) had an ectopic pregnancy in a rudimentary tube, which is frequently present in these cases, and this occurrence must be considered one of the rarer hazards of the anomaly. The remaining 4 abortions were spontaneous. One in 5 of the pregnancies recorded ended in abortion. Five of the 6 women who aborted had also had full-time pregnancies.

Of the pregnancies which went to viability, 2 patients were delivered by elective Caesarean section for associated congenital abnormalities, that of Tucker and Baker (1953) for pelvic deformity and that of Whittemore (1942) because an artificial vagina had been constructed. Cabanes and Jahier (1938) delivered their patient on one occasion by classical section for ante-partum haemorrhage. This complication occurred 3 times in 5 pregnancies in this case and post-partum haemorrhage and manual removal of placenta twice. All the infants were liveborn although the first died after a few hours. Birk's (1931) patient had 3 consecutive breech deliveries. All the other patients had normal deliveries. Cabanes and Jahier (1938) attributed the obstetric difficulties of their patient to the unicornate uterus, and Taber (1950) believed that the small size of a 42-weeks infant in his case was due to the congenital defect. In both instances, however, this view was arrived at retrospectively.

Menstruation in unicornate uterus is reported to be normal, or scanty, painful and irregular. In 15 cases, where menstruation is mentioned, 3 had never menstruated, 3 had scanty painful periods, 4 had heavy painful periods and 5 had normal menstruation.

Clinically there is little evidence on which to base a diagnosis of unicornate uterus although a number of writers have noted deviation of the uterus to one or other side of the pelvis (Dannreuther, 1923; Whittemore, 1942; Taber, 1950) on bimanual examination.

Much interest has centred round those cases of unicornate uterus which are associated with renal agenesis on the defective side. Although Collins (1932), in tabulating a list of congenital anomalies mentioned in the literature as being associated with cases of renal agenesis, gives the number of cases of unicornate uterus as 60, Schumaker in 1938 was able to find only 28 authenticated cases in the literature. Since that time 10 further cases have been published and the case reported above brings the total of such cases to 39.

Schumaker (1938), in an extensive review of the subject, points out that numerous authors have called attention to the frequent association of congenital abnormalities of the genital and urinary systems, and emphasizes the need for investigation of the renal tract where genital abnormalities are found, and vice versa, a point which is also emphasized by Jarcho (1946). In the opinion of Guttierrez (1933) it should be assumed that the absence of the vagina or uterus or any other important anomaly of the genital tract in the female suggests the probability amounting almost to a rule that there is congenital absence of one kidney. It must be

noted, however, that by no means all of the cases of unicornate uterus here reviewed conform to this rule. Schumaker (1938) estimated that, if renal agenesis was present, in 70 per cent of the cases there was also a major genital malformation. Conversely he quotes Anders (1910) who found that, where a genital malformation is present, 90 per cent of the cases also suffer from renal agenesis on the defective side. A more recent pronouncement is that of M. Campbell (1951), who estimated that upper urinary tract anomalies appear in one-third of cases with major genital malformation. In the cases of true unicornate uterus now reviewed over 70 per cent had associated renal agenesis. Three further cases had ectopic, rudimentary and U-shaped kidney.

The defect would appear to be more common on the left side, which accounts for 25 (64 per cent) of the cases.

From an obstetric point of view the crucial factor must be the functional state of the remaining kidney. Guttierrez (1933) has stated, however, that regardless of the anatomic position the single organ may occupy it is nearly always potentially affected with some chronic disease, e.g., nephritis, pyelitis, pyelonephritis or other types of associated pathological process predisposing to urinary stasis. Owing to the lack of drainage, plus infection, hydronephrosis and stone formation are common, terminating in anuria, fatal uraemia and death. The cases described by Brackenbury (1891), Schattenburg and Ziskind (1940), Daro, Gollin and Nora (1950), Ostry (1950) and the case reported in this article died in this manner. In addition hypertrophy of the single kidney was noted in a few instances (Duncan, 1933; Schumaker, 1938; Varino and Beacham, 1941). Tucker and Baker (1953) reported a moderate hydronephrosis. Unicornate uterus associated with renal agenesis should thus be considered a potentially serious condition in pregnancy, and adds point to Ungerleider's (1952) statement that the gynaecologist and urologist must be cognizant that, when an anomaly of either tract is found, an associated abnormality may be present and the investigation of the possibility is important.

Besides the absence of derivatives of the Müllerian duct and the embryologically closely related derivatives of the Wolffian duct, unicornate uterus has been reported in association with other congenital defects. Ungerleider (1952) and Tucker and Baker (1953) described 2 cases in which the genito-urinary anomalies were associated with malformation of the bony pelvis. The pelvic inlet was obliquely elliptical with anterior rotation of the entire pelvis on the defective side. The ilium on the defective side articulated with the transverse process of the 5th lumbar vertebra, and the former authors considered the pelvic abnormality to be due to the failure of the ilium to descend caudally and articulate with the first sacral vertebra. Both cases had a lumbar scoliosis to the defective side and also spina bifida occulta.

Few authors have noted the presence or absence of the suprarenal gland but Guttierrez (1933) has pointed out this organ has a twofold origin, the cortex being developed from columns of cells from the Wolffian duct and the medulla in association with the sympathetic nervous system. Hence where the kidney is absent one assumes a suprarenal lacking one essential element.

In only 5 cases (Dannreuther, 1923; Varino and Beacham, 1941; Whittemore, 1942; Alexander, 1947; Ogilvie, present case) has there been renal agenesis with complete absence of tube, round and broad ligaments and ovary. The defect in each case was on the left side and Whittemore's case also had a congenital absence of the vagina and an anomaly of the 9th rib on the defective side.

The ovary is frequently present on the side of the abnormality but tends to be longer, narrower and more vertical than on the normal side, the blood vessels entering by the upper pole. It usually occupies an ectopic position, either above the pelvic brim or in the region of the ilio-inguinal ring. Its ligament, where described, extends to the ring. Neerhut (1954) attributes this low position of the ovary to a purely mechanical effect. The round ligament has remained free for a greater length of time and consequently has been able to pull the ovary down in the pelvis before it becomes attached to the first part of the uterus which it meets, viz., the cervix, which in these cases must

originate from the opposite Müllerian duct. The round ligament when present is usually a poorly developed structure attached to the cervical portion of the uterus.

The Fallopian tube when present is mostly a rudimentary structure, represented by a portion of the fimbriated end. It has been reported solid, but where it has become canalized it may be the site of an ectopic pregnancy (Taber, 1950), the presence of the fertilized ovum in this site being explained by intra-abdominal transmigration of spermatazoon or fertilized ovum. The broad ligament is usually represented by a thin remnant of the lower portion.

Numerous theories have been advanced to explain congenital anomalies of the female genital tract. Falls (1939) held that hormonal failure is responsible for improper fusion of the two halves of the system and other malformations. Anderson (1943) believed that many anomalies could be explained on the ground that the Müllerian duct on the left side advances ahead of the right and therefore an error in timing leads to malformation. Another theory suggests that defective germ plasma and unfavourable embryonic environment are the most important factors. DeLee and Greenhill (1947) attribute the abnormalities to lack of fusion, or rudimentary development, or suppression of development of one duct. Schumaker (1938) supports this theory and states that true unicornate uterus is due to real agenesis of the entire Müllerian duct, where no Fallopian tube is present, and to almost complete agenesis where the fimbriated end of the tube is present. Dannreuther (1923) suggested that total absence of half the genital apparatus must be due to prenatal arrested growth, but thought that partial development could result from foetal peritonitis. Schumann (1936) has pointed out that parallelism exists between various types of uterine anomalies in women and the normal genital organs of animals lower in the developmental scale. Blair Bell (1934) was impressed by this theory and suggested the term "Atavism" in preference to malformation. While he conceded that unicornate uterus is normal in birds he considered that this abnormality could not be considered an atavism but was the result of total suppression of one Müllerian duct.

No theory however explains all the various degrees of malformation and Neerhut (1954), in an interesting paper on the subject, points out that the precise pathogenesis must remain a mystery, although it is possible to deduce the mechanism of the malformation by an analysis of the underlying defective tissue organization. In discussing the mode of production of the defect in the case described by him, which had renal agenesis, unicornate uterus with rudimentary tube and ectopic ovary, he stresses the importance of the pronephric duct in the development of the genito-urinary system and quotes experimental evidence showing that sectioning of the growing Wolffian duct produces absence of the mesonephros, metanephros and ureteric bud in the renal system, and unicornate uterus and almost complete absence of the Fallopian tube in the genital system. He concludes therefore that the growing Müllerian duct is completely dependent on the Wolffian duct either for guidance or for a supply of cells, and should the growth of the pronephric duct be interrupted at any point, then that of the Müllerian duct also ceases at that point. He concludes that the anomalies described were due to some interruption of growth of the Wolffian duct between the pronephros and ureteric bud, or temporarily between the 4th and 6th weeks of intra-uterine life.

He points out that very similar malformation would have resulted if the pronephros itself had failed to develop but such an occurrence would likely be associated with other developmental anomalies outside the genito-urinary tract. In this case the interruption of growth would be even earlier in intra-uterine life, probably at the 2nd or 3rd week. The cases of Ungerleider (1952) and Tucker and Baker (1953) may possibly fall in this category.

As pointed out above Neerhut (1954) ascribed the ectopic ovary to purely mechanical forces in his case but this explanation does not fit those cases in which the ovary on the defective side occupies a normal position or one above the pelvic brim.

Embryologically therefore unicornate uterus must arise from some factor acting on a small area of the developing foetus for a short period in the 4th to 6th week of int a-uterine life or

even earlier where there is evidence of complete agenesis of the pronephros.

Summary

A case of true unicornate uterus associated with renal agenesis is reported.

The literature is reviewed.

An attempt is made to assess the frequency of pregnancy in this anomaly.

The potential danger of pregnancy as a result of the renal agenesis is stressed.

The embryology of the anomaly is discussed.

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TWO CASES OF EXCESSIVE UTERINE HYPERTROPHY FOLLOWING ON PROLONGED OESTROGEN ADMINISTRATION

BY

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WITH the advent of the synthetic oestrogens, whether in the form of stilboestrol, ethynal oestradiol, etc., the use of these hormones has increased very much, and the indications which have been given for their administration have widened considerably. While the foremost of these remain the vasomotor instability associated with the climacteric, and manifested as "hot flushes", these hormones are now used in the treatment of many less well defined symptoms which may or may not be associated with the menopause, the duration of which has become increasingly elastic. They are also employed in the treatment of such widely varying conditions as types of arthritis, skin diseases, etc. In this way many patients are receiving oestrogens in rather indiscriminate dosage over varying periods of time, and often without adequate supervision or warning of the possible ill-effects which may be produced by their prolonged use or sudden withdrawal.

Most gynaecologists are familiar with the problem set us by this type of patient when unaccompanied by exact data from the doctor referring the case. It has been found by myself and my colleagues working in a large gynaecological department, that some patients appear to develop what might almost be called an "addiction" to oestrogens, and these have come to be known by us as "oestrogen eaters". A series of endometria from menopausal and postmenopausal patients receiving oestrogen, with controls, has now been studied by myself and a colleague, Dr. Anne Gibson, and is being continued by the latter who hopes to publish her results in due course, and to whom I should like to express my grateful thanks for help with the pathological side of this paper. From this investigation it is evident that a varying degree of cystic hyperplasia is frequently present in such patients, the proportion of endometria showing this change being very much higher than is found in controls.

Dr. Bamforth (1956) in a recent paper draws attention to the co-existence of cystic hyperplasia and endometrial cancer, both being present in 17 cases out of a series of 81 cases of this latter condition. This association has also been found in sections studied by us, and is present not only in cases of "spontaneous hyperplasia" (Fig. 1), but also in endometrial hyperplasias presumably induced by the administration of oestrogens (Fig. 2). As a rule the degree of hyperplasia produced by the administration of oestrogen is moderate (see Fig. 3), and the uterus is not grossly enlarged, nor does the presence of withdrawal bleeding bring the patient to urgent operation.

In the last two years, however, 2 cases have come under my care illustrating a uterine hypertrophy (myometrium and endometrium) of such magnitude that I feel their publication may be of interest, more especially as I have not been able to find descriptions of similar cases in the literature.

Case 1, Mrs. M., aet. 61, was referred by her doctor as she was continuing to have profuse and irregular periods.

Past history was not relevant to the present complaint.

Present history. For the past 4 years the periods have been increasingly excessive, lasting 10–14 days and appearing at irregular intervals from 2–8 weeks. At some time the patient had been given stilboestrol, and, finding that this hormone tended to cut short a heavy loss, had

been taking oestrogen tablets intermittently for the past 4 years. Indeed she was taking a tablet of stilboestrol at any time she thought a loss might occur and be inconvenient, such as "going to the pictures".

Condition of examination. There was no anaemia; the haemoglobin was 90 per cent.

Pelvic examination. The uterus was anteverted and very bulky. The cervix was eroded and unhealthy. The fornices were clear. The provisional diagnosis at the time of consultation was: bleeding associated with a small granulosa cell tumour or due to hyperplasia associated with oestrogen administration.

Treatment. Panhysterectomy with removal of both appendages was carried out.

Operation specimen. The uterus was the size of a 10-weeks pregnancy, the cavity to the external os measuring 11 cm. The fundus was broad, tending to the bicornuate type, and the uterine walls were extremely thick, the anterior wall measuring 3·25 cm. and the posterior wall more than this. At some areas the myometrium shows cystic and yellow-stained spaces. The endometrium formed a thick white layer, firm, with a rough polypoid appearance towards the uterine cavity. The ovaries and tubes were normal.

Histology. Portions of the myometrium show adenomyosis. The endometrium shows a marked cystic hyperplasia (see Fig. 4, Case 1). Many of the cells lining the glands are of a pale type. There is no evidence of malignancy.

Case 2. Miss M., aet. 55, was admitted as an emergency on the 12th March, 1956 at the request of her doctor.

The *past history* was not relevant.

History of present illness. For the past 5 years the periods have been increasingly scanty and spaced out, and during this time there have been intervals of amenorrhoea up to 6 months in duration. For the past 3 to 4 years "hot flushes" and night sweats have been increasingly troublesome, and the patient has been taking oestrogen in the form of ethynal oestradiol at irregular intervals for the whole of this time. The commencing dose was 0·1 mg. daily, but this was soon increased to 0·5 mg. daily and withdrawal bleeding took place on several occasions. Apparently this dosage was continued up to about 6 weeks prior to admission, and withdrawal bleeding occurred on 28th February, becoming heavy on 29th February, and has continued ever since.

On the day of admission it was extremely heavy, and was accompanied by abdominal pain, and the patient was admitted to hospital.

Condition. The patient looked pale and ill. The haemoglobin was 58 per cent.

Pelvic examination. Profuse bleeding was present, and the vagina was filled with clot. The uterus was definitely enlarged, the cervix closed and thinned out, the cervical canal being distended with blood clot.

Examination under anaesthesia confirmed the above findings, and in addition a finger passed through the cervical canal felt an irregular polypoid mass just above the internal os.

Diagnosis. The possibility of a sarcoma of the uterus was considered, but remembering Case 1 it was thought that the probability was a hyperplasia induced by oestrogen. A total hysterectomy and removal of both appendages was carried out, a transfusion of two pints of blood being commenced in the theatre.

Operation specimen. The uterus was the size of a 10–12-weeks pregnancy (Fig. 5, Case 2), measuring 11·5 cm. to the external os. The uterine wall was 2 cm. thick at the fundus, one-half of this being composed of thick white endometrium which was attached to the myometrium along a very straight line without, however, appearing to penetrate it (Fig. 6, Case 2). At the lower end of the uterus, the endometrium ends in a ragged free border to the right of which there is a small area of thin normal-looking endometrium.

Histology. The endometrium shows marked hyperplasia with glands closely set together right down to the myometrium (Fig. 7, Case 2). There are also areas of squamous metaplasia. Areas of cystic endometrium exist and there are a large number of the pale cells described in the former case (Fig. 8, Case 2). There is no evidence of malignancy. The left ovary showed a follicle cyst. The right shows no abnormality.

Comments

An account has been given of two cases of uterine hypertrophy associated with prolonged

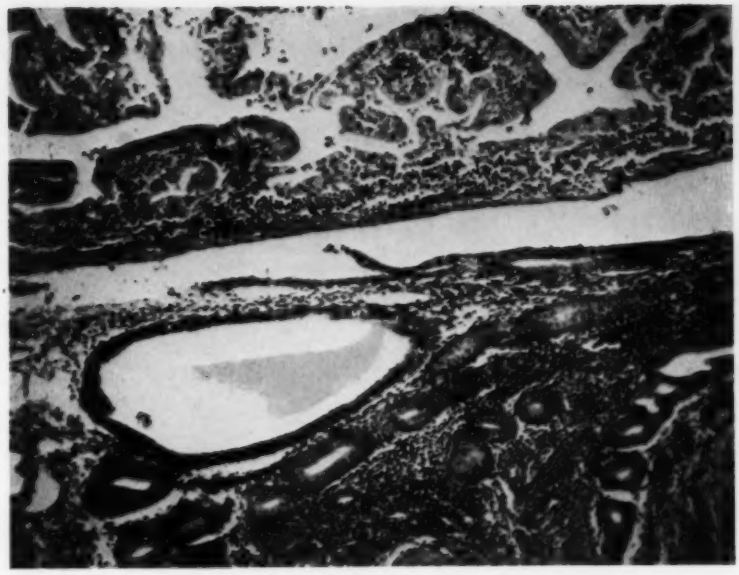

FIG. 1

Endometrium showing co-existence of hyperplasia and carcinoma from a woman who had received *no* oestrogen. H. & E. ×128.

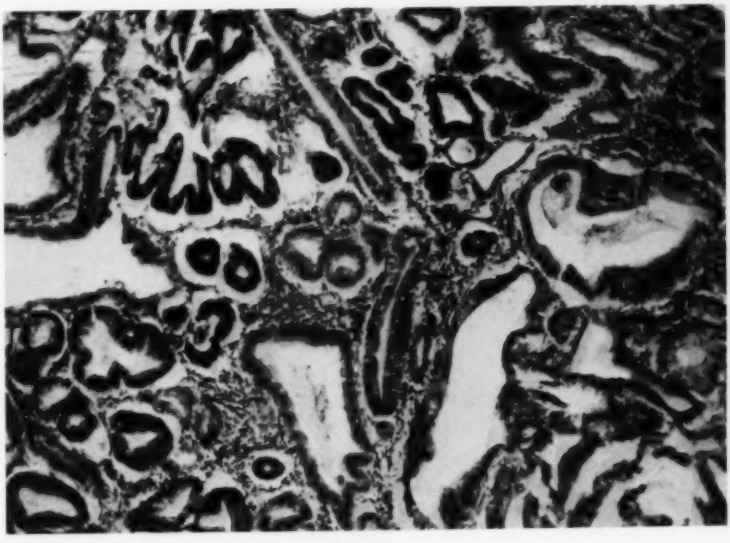

FIG. 2

Endometrium showing co-existence of hyperplasia and carcinoma in a woman who had taken oestrogen more or less continuously over several years. H. & E. ×120.

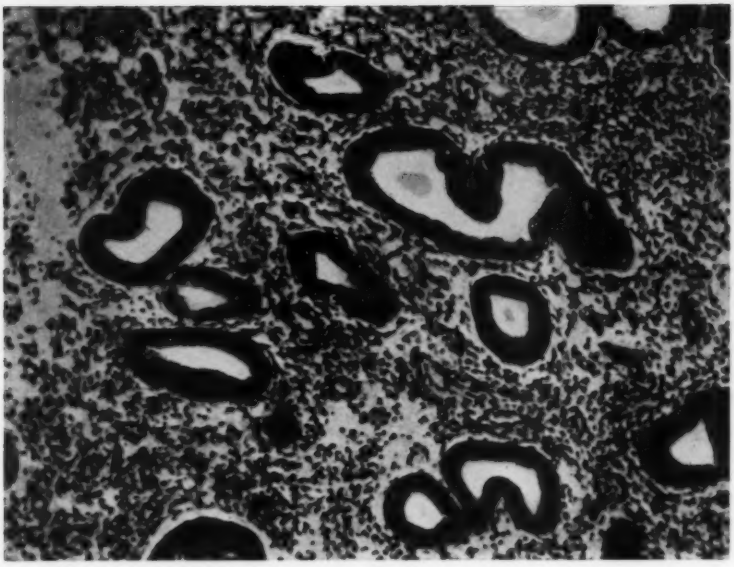

FIG. 3

Endometrium showing usual moderate degree of hyperplasia induced by oestrogens. H. & E. ×128.

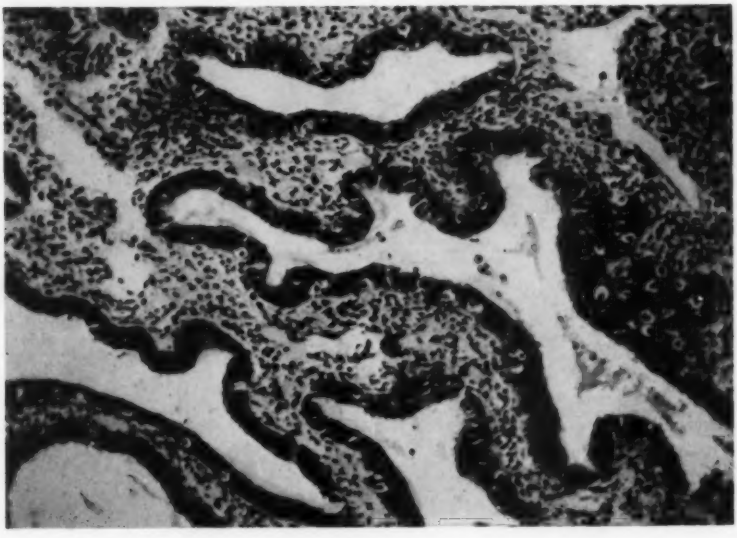

FIG. 4

Endometrium from Case 1 showing marked cystic hyperplasia and many pale, florid cells. H. & E. ×120.

A.B.

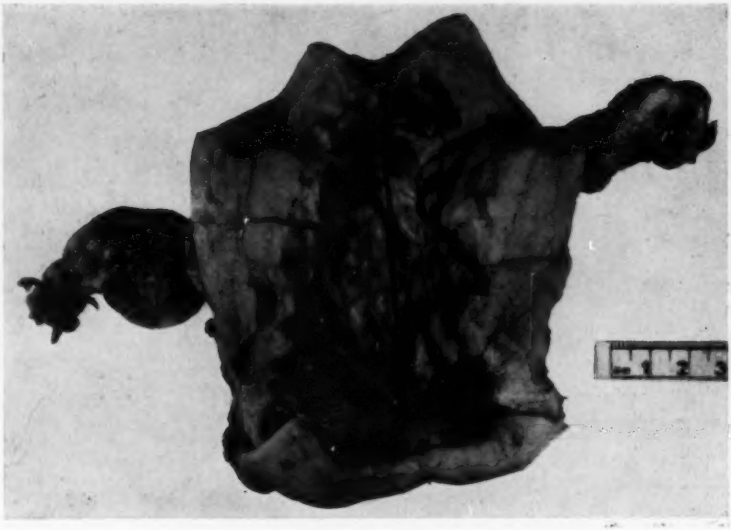

FIG. 5

Operation specimen from Case 2. Note extreme thickness of uterine wall about half of which is formed by endometrium.

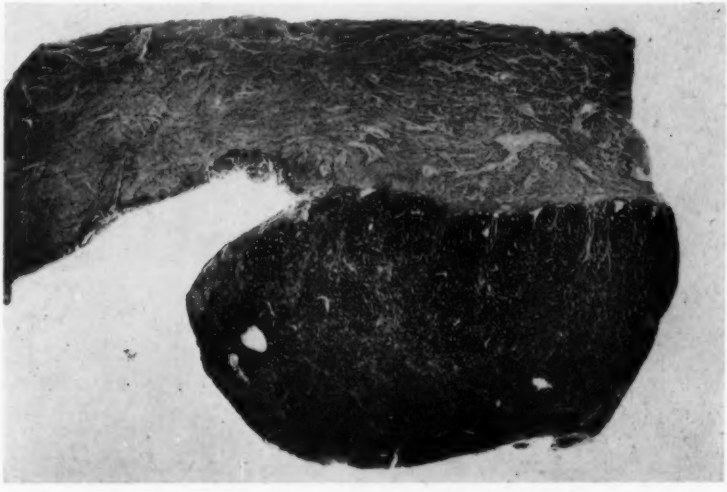

FIG. 6

Section of uterine wall from Case 2 showing enormous thickening of endometrium in relation to uterine wall. H. & E. ×4·5.

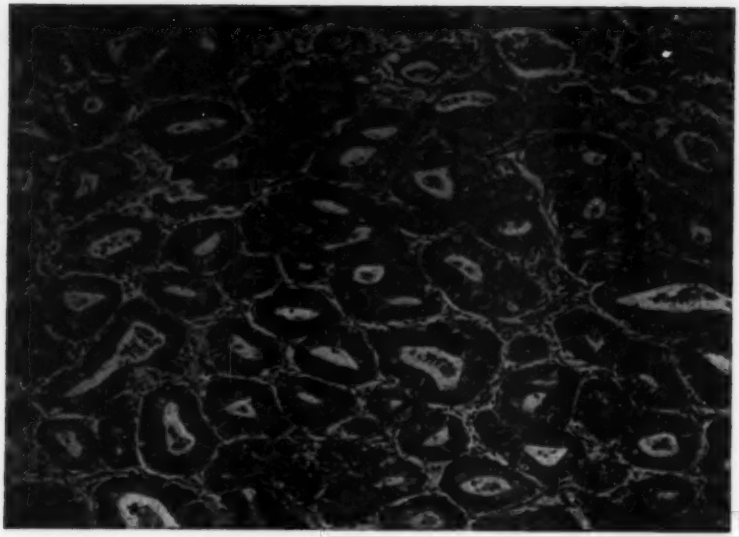

FIG. 7

Endometrium from Case 2. Note intense glandular hyperplasia. H. & E. ×120.

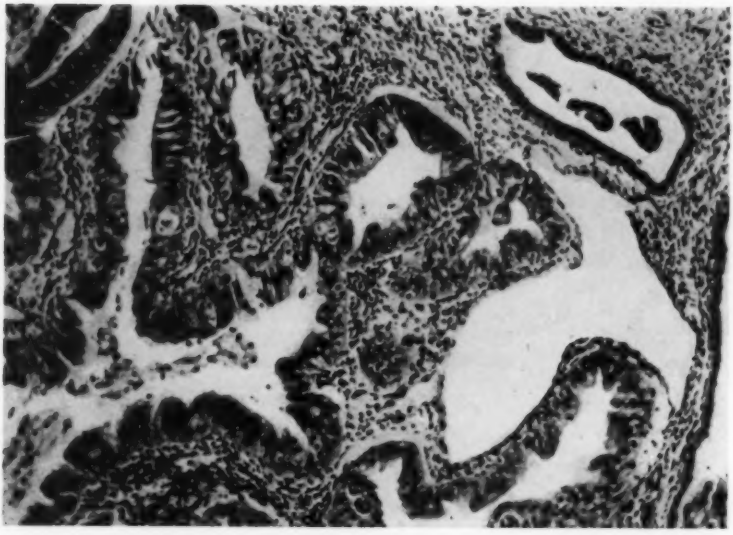

FIG. 8

Section of endometrium from Case 2 to show tall pale glandular cells mentioned in text. H. & E. ×120.

A.B.

administration of oestrogen. While the site of the most dramatic hypertrophy is the endometrium, the myometrium is also involved, causing a very considerable enlargement of the organ. In both cases a very marked cystic hyperplasia of the endometrium has been produced, and both, especially Case 2, show many of the "pale" eosinophil glandular cells described by Bamforth and others, and considered by this former writer as a possible transitional stage in the development of cancer. In neither of these cases, however, had any malignant change developed in spite of the extent of the endometrial hypertrophy.

Figure 2 is from another patient who had taken oestrogens for a similar prolonged period, but in whom no uterine hypertrophy was present. The endometrium shows both an adenocarcinoma and hyperplasia.

Dr. Bamforth in his recent paper found 17 out of 81 cases of carcinoma coexisting with metropathia, and it is generally agreed a relationship exists between the two conditions. It would appear logical to assume that a similar relationship exists between the hyperplasia induced or increased by the administration of synthetic oestrogens and carcinoma, and in the light of this assumption it is difficult to understand the different pictures as shown in Figure 2 and Figure 7 both from women in the middle fifties receiving an approximately similar length of exposure to this hormone. In the former the uterus remained very small and contained a carcinoma and hyperplasia. In the latter an enormous uterine hypertrophy is present but no carcinoma.

Fremont-Smith, Meigs, Graham and Gilbert (1946) suggest that oestrogen stimulation may be one factor in the chain of processes resulting in carcinoma. Winter (1952) is of the opinion that a definite relation exists between the stimulation of oestrogen and the development of carcinoma, and that, while as a rule large doses given over a long time are required, carcinoma will sometimes appear after small doses. He considers that oestrogen may be an activating agent in carcinoma-prone endometrium.

Summary

Two cases are described in which a very marked uterine hypertrophy is associated with prolonged oestrogen administration, the resultant excessive haemorrhage necessitating hysterectomy. A third case is mentioned where prolonged oestrogen therapy was associated with no uterine hypertrophy, but the endometrial hyperplasia was associated with an endometrial carcinoma.

In conclusion, it would seem necessary that any patient receiving the synthetic oestrogens should be carefully supervised and the dosage regulated, and that prolonged treatment with heavy dosage should be avoided.

I should like to express my thanks to Dr. J. B. Walter of the Royal College of Surgeons, who has so kindly made the photomicrographs for me.

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HYSTEROSALPINGOGRAPHY WITH ENDOGRAFIN

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ALTHOUGH hysterosalpingography is a comparatively safe procedure, there are known dangers and these appear to be higher when an oily medium is used to outline the cavity of the uterus and tubes. The risk of reactivating a quiescent pelvic infection is as high as 1 per cent of all cases when such a medium is used. Moreover, an oily preparation can, if retained in the tubes or in a peritoneal pouch formed by adhesions, take many months to absorb (Fig. 2) and in the meantime may theoretically if not actually induce a foreign body reaction in the tissues. Some authorities allege that such a reaction can occur in a normal and patent genital tract, and, although this is not proved to the satisfaction of all, oil granulomata in the uterus, tubes and peritoneal cavity are recorded.

Despite all precautions intravasation occurs in 1 to 2 per cent of cases of hysterosalpingography and, although it rarely produces clinical manifestations, even when an oily preparation is injected, it is a good reason for using, if possible, a radio-opaque solution which is harmless even if it enters the blood stream.

In view of such considerations various rapidly absorbed water soluble media were introduced for hysterosalpingography during recent years, only to be withdrawn after a short time in vogue, when doubts were cast on the safety of their constituents. All have suffered the disadvantage that their rapid absorption from the peritoneal cavity has made them unreliable in the diagnosis of peritoneal adhesions. We have tried such media but have abandoned them on account of technical difficulties and uneven results.

Erbslöh (1955) recently introduced a new substance which is now marketed under the name of "Endografin" by Schering, A. G., Berlin. This is the methylglucamine salt of N:N'-adipic-di-(3 amino-2:4:6 triodobenzoic acid) in 70 per cent solution. The manufacturers say that it contains no additives for increasing viscosity; these have been the source of trouble with other aqueous products (Bergman, Gorton, Norman and Sjöstedt, 1955). It is also stated to be chemically identical with "Biligrafin" though the concentrations differ. "Biligrafin" is a contrast agent for intravenous cholecystangiography, and although reactions have been reported it is regarded as safe (Sutton and Tillet, 1954) and is now widely used. It is thus reasonable to assume that Endografin also is safe for use in hysterosalpingography and we decided to give it a trial.

METHOD

The technique used in these cases is a simple one. First the patient is catheterized, placed on a comfortable ambulance and given Pethidine, 100 mg., intramuscularly. One hour later she is wheeled to the X-ray Department and, after removal of the catheter, she is placed on the examination couch in the left lateral position. A Sim's duckbill speculum is inserted, the vagina is swabbed with 2·5 per cent Dettol solution and then dried carefully. Iodine is best avoided as in our experience 2 cases of exfoliation of the vaginal skin followed its use. The cervix is seized with a single vulsellum and brought into view. A suitably sized Leech Wilkinson cannula

is then screwed into the os without the preliminary use of a uterine sound. Passing a sound predisposes to intravasation and is not necessary with this type of cannula. The speculum is removed and the patient adopts a supine position before injection of the Endografin. Manometric control is not used but the injection is watched on a fluorescent screen by both radiologist and gynaecologist. Films are exposed at intervals judged by screening; the usual number being two or three. If tubal patency is not shown the patient is given a sublingual tablet containing 1/120 gr. of glyceryltrinitrate. To achieve the best results it is important to use a cannula which fits the cervix accurately. Reflux through the cervix can also be avoided by not overheating the medium for its viscosity decreases by one-third between the temperature of 20° and 37° C. (Erbslöh, 1955) and poor uterine filling and air bubbles result; this was seen in two cases. A full explanation of the various stages of the operation is given to the patient some time previously, and this goes far to reduce apprehension and discomfort. Our experience with Endografin is so far limited to 20 cases but the findings are of such interest that it appears justifiable to report them.

Radio-opacity

The outline of the uterine cavity and that of the Fallopian tubes is comparable in density with that seen by other methods (Fig. 1). In particular the details of the isthmus and internal os are well demonstrated. Of the 20 cases in this series satisfactory uterine filling occurred in all but the 2 cases mentioned above.

Absorption

Peritoneal spill is best demonstrated immediately by changing the position of the patient whilst she is under the screen, and can sometimes be accelerated by moving the cervix with its cannula. If spill is not shown by this manœuvre a further exposure is made after 30 minutes (Fig. 3); to delay longer is a disadvantage because the medium is rapidly absorbed. Films exposed at 30-minute intervals in two cases demonstrated that the pelvis is clear after 3 hours. Since then we have routinely taken a pelvic radiograph at 4 hours and confirmed that absorption is normally complete at that time. In only 2 cases was there any pelvic residuum after 4 hours; both these patients had blocked tubes and in neither was there a 4-hour cholecystogram.

It was feared that rapidity of absorption would be a disadvantage from the standpoint of demonstrating peritoneal adhesions, or as Murray and Martini (1946) describe it, "pelvic block". In fact the presence of peritoneal pockets reduces the speed of absorption sufficiently for opacities to persist for 24 hours, and absorption from such pockets is only complete in a few days. If the opacities are intratubal they tend to increase in size during the first few hours. The calculated osmotic pressure of Endografin at body temperature is approximately 23 atmospheres and the increase in size is probably due to extraction of fluid from the plasma, but this does not appear to cause any symptoms.

At first an examination of radiographs taken 4 hours after injection may be somewhat confusing. This is because the material is retained in the vaginal vault, outlining the cervix and in fact demonstrating the vaginal rugae (Fig. 4). Absorption from the vagina does not occur or only occurs slowly and this contamination can be cleared by gentle swabbing of the vagina with ½ per cent Cetrimide solution.

Excretion by the Liver

In the absence of liver damage 90 per cent of Biligrafin, given intravenously, is excreted through the bile ducts into the bowel (Aldridge, 1955). The more concentrated Endografin used for hysterosalpingography is also excreted in this manner. Reviewing the serial radiographs for Cases 3 and 4 we found that the substance reached the common bile duct in one hour (Fig. 5), the cystic duct and gall bladder in two hours and the small bowel in three hours. A 24-hour film showed the material in the large bowel (Fig. 6). Clinically this excretion into the bowel can produce 2-days constipation and some colicky abdominal pain, but these symptoms are unusual unless more than 10 ml. have been injected. In 13 patients the medium was seen in the large bowel after 24 hours, no film was taken in Cases 1 and 10 and no absorption had occurred in 4 of the remaining 5.

It might be expected that a clear cholecystogram would require a high dosage of Endografin. Whilst it is true that dense bowel shadows are obtained by using up to 15 ml. nevertheless a good gall bladder shadow has been obtained with as little as 5·5 ml. The quantity used has varied: 6 patients had more than 10 ml., 11 had between 7·5 and 10 ml. and 3 had less than 7 ml. Probably more significant than dosage is the effect of premedication. Morphine was used in two cases and pethidine in 11 cases. Pethidine has been routinely used for hysterosalpingography at this hospital for some years and it was not at first appreciated that it might directly affect the results obtained with Endografin. However, it has been shown that pethidine and morphine greatly improve the standard of cholecystography by contracting the sphincter of Oddi (Aldridge, 1955), and for this reason methylpentynol was used as a control in 7 cases. After allowing for other variables the findings seem to confirm the improvement Aldridge claimed.

Apparently absorption does not occur from the uterine cavity or from peritoneal pockets at a rate sufficient to produce a good cholecystogram, but only from the free peritoneal cavity. For this reason we accept a good gall bladder shadow, seen at 4 hours or earlier, as evidence of tubal patency and intraperitoneal spill. Conversely, the absence of a cholecystogram suggests blocked tubes, but only if liver function is normal. This was well illustrated in 4 cases in which, following failure to demonstrate tubal patency, no cholecystogram was seen. In Case 9 there was doubtful spill and the gall bladder shadow was weak and was not present at 4 hours. Of the remaining 15 cases, all were shown to have full intraperitoneal spill on fluoroscopy, in 2 the gall bladder was not examined at 4 hours but in 13 cases it was clearly seen. Where the fluorescent screen is not used a view of the gall bladder at 4 and 24-hours should be of great assistance in assessing intraperitoneal spill.

Sequelae

So far the discomfort suffered by the patient seems to be less than with other media. Three patients were known to have a degree of non-tuberculous pelvic infection when they requested investigation, but no reactivation of salpingitis has yet occurred. Two patients were subjected to laparotomy, one 4 weeks and the other 6 weeks after hysterosalpingography; no peritoneal changes were seen which could be attributed to the Endografin and there were no granulomata. Indeed there have so far been no general or local reactions and it is hoped that the morbidity will prove to be lower than the overall figure of 1 per cent quoted by Jeffcoate (1951). In this respect it should be noted that all patients in this series had previously been investigated for the presence of tuberculous endometritis, with negative results.

Conclusions

Over a small series of cases no complications have occurred following the use of water soluble Endografin for hysterosalpingography. Uterine and tubal outline, peritoneal spill and pelvic block can all be demonstrated with this new medium. Cholecystograms can be produced as part of the investigation and are of value in assessing tubal patency.

We wish to thank Professor Jeffcoate and Dr. Whitaker for permission to undertake these investigations and to publish the results. We are also indebted to Schering, A. G., Berlin, for samples of the product and to Mr. Norman for the reproductions of the radiographs.

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FIG. 1

Combined hysterosalpingography and pelvic pneumogram. There is free spill from the tubes.

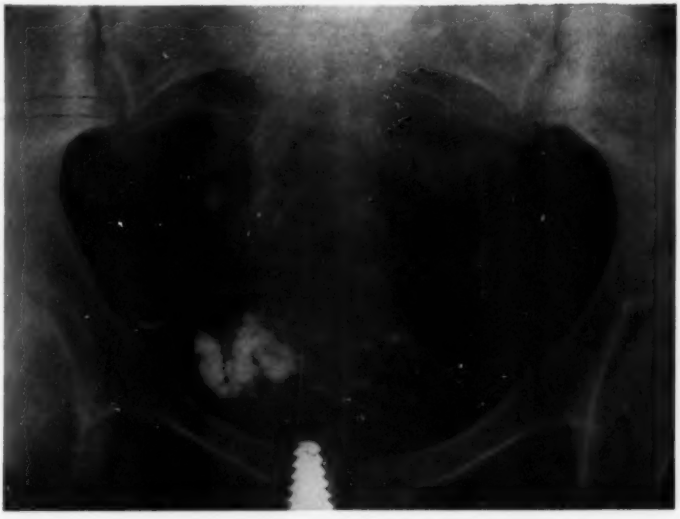

FIG. 2

Film taken 6 months after hysterosalpingography with oily medium. Cannula is in position for repeat investigation but no oil has been injected.

FIG. 3

The Endografin has spread freely; there is some distortion due to a left-sided ovarian cyst.

FIG. 4

"Vaginogram." The rugae of the lower vagina can be seen. The right fornix is outlined and the cervix is shown as a negative shadow.

FIG. 5

Case 3. The common bile duct is outlined one hour after hysterosalpingography.

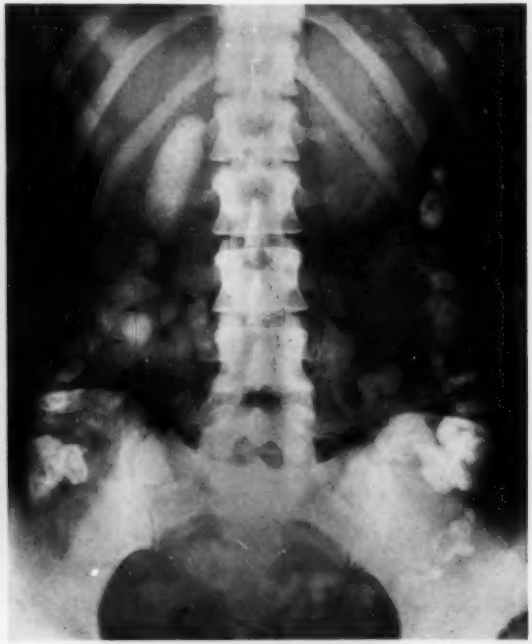

FIG. 6

Case 2. A clear cholecystogram is seen in a 24-hour film. The large bowel is also outlined.

PARAVERTEBRAL SYMPATHETIC BLOCK IN THE TREATMENT OF SUPERFICIAL AND DEEP THROMBOPHLEBITIS OF LEG VEINS

BY

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PARAVERTEBRAL sympathetic block first applied by Leriche and Kulin (1934) has been described as one of the most reliable and successful methods of treatment of thrombophlebitis (Mandl, 1947). Numerous papers have testified to its value in cases of deep thrombophlebitis but we have found it to be of value also in the similar superficial lesions, particularly in those where the condition has been progressive, tending to spread along the line of a vein.

The clinical picture of thrombophlebitis is due in part to venous spasm, to enlargement of the clot in the vascular lumen and to arterial spasm. The last is generally regarded as the main cause of pain, but Mandl (1947) considers this to be due rather to the venous spasm, which contributes to further coagulation. Ochsner and DeBakey (1950) have shown that spasm gives rise to lymphatic obstruction in the perivenous segments and may be so severe as to lead to gangrene of the extremities. Perivenous lymphatic obstruction also plays a part in producing oedema, which is further aggravated by raised intravenous pressure and increased capillary permeability due to anoxia leading to a rise in the perivascular tissue fluid. Venous pressure is raised to as much as four or five times normal (Ochsner and DeBakey, 1950).

Paravertebral block acts immediately by relieving venous and arterial spasm. This in turn decreases the venous pressure and so the filtration pressure. Arterial pulsation returns to normal and oxygenation of the endothelium and increased lymph flow are both re-established. In many cases a single injection will produce permanent relief but other cases require two or more injections at 24- to 48-hour intervals. Some authors such as Mandl (1947) have described the use of 6 to 10 treatments as routine, while Ochsner and DeBakey (1950) recommend up to 6 injections.

As disadvantages of the method Mandl (1947) states that every new injection puts the already nervous patient into a renewed state of excitement. In an attempt to avoid this, Ansbro and Mendoza (1950) have used a continuous paravertebral block injecting procaine penicillin through a polythene catheter. This carries a risk of infection and in one of their cases a lumbar abscess formed requiring incision and drainage. Steele (1951) has obtained good results with continuous caudal block in chronic cases and recommends that active muscular movements should be promoted to assist the work of the venous tree. Gravelle (1949) considers that, although paravertebral infiltration is a definite adjunct in treatment, it may give a false sense of security, and may even promote pulmonary embolus. He describes 2 cases, each having had 6 paravertebral injections, one of whom died from pulmonary embolus, and considers that vein ligation is the only certain method of excluding this complication. Steele (1951) however states that once the signs and symptoms of femoral and iliac thrombosis appear the danger of pulmonary embolus is comparatively rare. Mandl (1947) also suggests that the rapid relief of symptoms may induce

undue shortening of the period of immobilization but Boyd (1948) states that immobilization is, in any case, the worst possible treatment in that it slows the circulation and ensures extension of the clotting process.

Advantages of the treatment are that it is simple and safe and can be carried out in any surroundings in contrast to the use of anticoagulants. Boyd (1948) and Browne (1954) suggest that the method is within the scope of any practitioner but it is a technique which, for good results, requires practice, and we have found it here best carried out by members of the anaesthetic staff. As an interesting alternative method Hollis, Holoubek and Chanton (1948) suggest tetraethylammonium chloride as a ganglion blocking agent but, although they found an improved blood flow to the lower extremities, the results were only temporary and were less marked than those obtained with lumbar sympathetic block.

The best results are probably obtained if the block is performed immediately the condition is recognized (Manuel, 1946; Browne, 1954) but Ochsner and DeBakey (1950) obtained good results in treatment undertaken from one to twenty-eight days after the onset of the condition and even in chronic cases, especially where peripheral circulation is impaired due to vasospasm. Boyd (1948) considers the method worth a trial. Mandl (1947) considers that the venous spasm may continue for months or even years. Papper, Aleison and Immlet (1944), investigating two cases of chronic thrombophlebitis by venography, were able to demonstrate venous spasm, and to show that it was relieved after paravertebral block.

Good results have also been obtained in phlegmasia cerulea dolens, a condition showing abrupt onset with rapid development of pain, swelling and cyanosis with massive oedema due to sudden massive intravenous coagulation (Wright, 1956). This condition has also been treated by opening the femoral sheath and carrying out periarterial sympathectomy (Sackenreiter, 1940).

Our aim has been to block the lower end of the lumbar sympathetic chain by means of a single injection and the technique used has been as follows:

The patient is placed in the lateral position with the affected leg uppermost. The spine of the third lumbar vertebra is identified and 4-fingers breadth lateral to it a skin wheal is raised. Through this a 12 cm. needle is inserted at an angle of 45° to the median plane of the body. If the needle is advanced slowly, and small amounts of local anaesthetic injected whilst doing so, very little, if any, discomfort to the patient will occur. When the side of the vertebral body has been felt the needle is withdrawn slightly and its direction altered so that when advanced again its point will slide past the antero-lateral surface of the body. A loaded 10 ml. syringe is now attached to the needle and, with slight pressure applied to the piston, the needle is slowly advanced. When the point of the needle emerges from the substance of the psoas muscle and enters the retroperitoneal space resistance to injection suddenly gives way and the piston moves as freely as in an intravenous injection. The aspiration test is then performed and, if negative, up to 30 ml. of local anaesthetic is injected. The particular anaesthetic used is immaterial; in our series we have used 0·1 per cent Amethocaine with 1 in 400,000 adrenaline.

The loss of resistance to injection experienced on entering the retroperitoneal space is quite definite and is comparable to that experienced on entering the extradural space by the Dogliotti technique (1933).

The accuracy of this method has been proved on a number of occasions by injecting a small quantity of dye (4 ml.) in patients undergoing lumbar sympathectomy and finding it in close proximity to the chain. In our opinion it is much more reliable than methods where the needle is advanced a fixed distance after contact is made with the vertebral body. We have found this distance to vary between 2 cm. and 3·5 cm. and it is obvious that, if the injection is made into the substance of the psoas muscle, it is unlikely to burst into the retroperitoneal space and reach the sympathetic chain.

In the Maternity Unit at Ronkswood Hospital active movement under the supervision of the physiotherapists has been carried out routinely in all cases and other measures, such as avoidance of constriction of the legs and prophylactic

anticoagulants where thrombophlebitis has previously occurred, have been employed. Despite all our care 13 cases of deep and 25 cases of superficial thrombophlebitis of the legs during the puerperium have occurred during the past three years, during which time there have been 2,344 deliveries (1·62 per cent).

Three of the superficial lesions were well localized and were successfully treated with local applications of kaolin which relieved pain and brought about resolution within 72 hours. Seven were treated with anticoagulants and all eventually settled down although pain persisted in all cases for 3 or 4 days and in some for considerably longer. Eleven cases were treated with paravertebral block alone and in 3 of these, where both legs were affected, bilateral block was employed. In all the above cases immediate relief of pain was obtained and the patient was at once able to move the leg freely and so promote rapid resolution of the condition which usually settled down within 3 days. In only one of this group symptoms recurred 2 days after the block had produced a dramatic initial relief and here anticoagulant therapy was instituted with cure over the course of the next 4 or 5 days. In 4 cases paravertebral block was used where the condition was continuing to spread and pain persisted in spite of adequate doses of anticoagulants for 4 days or more and in all cases arrest of the spread of the condition with rapid improvement was obtained.

Of the cases of deep thrombophlebitis, 5 were treated with anticoagulants alone and in one of these an abscess developed at an injection site in the thigh and took three weeks to heal. Seven were treated with paravertebral block alone which in 2 cases was repeated after 48 hours as the condition had not settled. One patient was admitted from another hospital with characteristic phlegmasia alba dolens with gross oedema of the leg, persistent pain and considerable pyrexia after three weeks treatment with anticoagulants. Following a single paravertebral block the condition rapidly settled down with immediate disappearance of pain, of pyrexia within 24 hours and of oedema within 72 hours. In only one of the group treated with anticoagulants a non-fatal pulmonary embolism occurred. This confirmed the findings of Steele (1951) and we have not shared the experience of Gravelle (1949) in this connexion, since none of our cases treated with paravertebral block suffered from this complication.

All our cases were eventually cured and little or no residual disability was found on subsequent examination. During the past year, however, we have come more and more to rely upon paravertebral block in treatment since it appears to offer several advantages over treatment with anticoagulants. These are (1) shorter overall recovery time, (2) immediate relief of pain and consequent freedom of movement of the limb, (3) its availability in the patient's home or in small hospitals where adequate laboratory facilities to control the use of anticoagulants are not available, (4) avoidance of risk of haemorrhage which occasionally occurs with anticoagulant therapy even where careful laboratory control is carried out. Mandl's objection to the mental strain imposed upon the patient by repeated paravertebral injections does not appear valid since we have rarely found more than one injection necessary and the performance of the block has not caused distress. The patients who have required a second block have been perfectly willing to submit to further injection. In view of reports of dangerous and even fatal haematoma formation in the paravertebral area, in cases where the block has been undertaken in patients already on anticoagulant treatment, we have proceeded with some caution and have not used the method where the prothrombin time was below 30 per cent of normal. This has involved delay, sometimes up to 24 hours but no longer. It is noteworthy that in the cases reported (O'Connor, Preston and Theis, 1950; Welti and Breynaert, 1951) repeated injections have been carried out and the prothrombin time has been about 20 per cent and 15 per cent respectively. In our series we have encountered no difficulty either with haematoma formation or with infection.

The value of this method in the treatment of deep thrombophlebitis has long been recognized but we feel that it has a definite place in the management of the superficial case also. It may be argued that the superficial case can be disregarded and does not require treatment but in many instances this condition can produce

severe pain and prolonged disability and, contrary to former belief, it may give rise to fatal pulmonary embolism (Stallworthy, 1956). Immediate relief of pain and rapid mobilization of the patient can be obtained with minimal disturbance and in some instances dramatic arrest of the spreading superficial phlebitis can be secured where, with other methods of treatment, the patient may be disabled for a long period.

Pulmonary embolism must always be regarded as the ultimate disaster in all conditions of thrombophlebitis and any form of treatment must aim at reducing the risk of this complication. It might be argued that paravertebral block, by reducing the venous spasm, may even tend to dislodge the clot and so promote spread to the lungs, but this has not been our experience. It would appear that treatment instituted early enough should even prevent the formation of a thrombus and this is, of course, a strong argument in favour of undertaking treatment at the first appearance of symptoms. Even where symptoms have been present for some time, however, in our experience the block can safely and profitably be used.

Summary

(*a*) Thirteen cases of deep and 25 cases of superficial puerperal thrombophlebitis are reviewed.

(*b*) All were treated successfully either with local applications, anticoagulants, or paravertebral block.

(*c*) Paravertebral block is recommended since it gives more rapid relief of symptoms and quicker recovery than other methods.

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THE TREATMENT OF ENDOMETRIAL TUBERCULOSIS WITH STREPTOMYCIN AND PAS

A SUPPLEMENTARY REPORT ON AN INVESTIGATION CARRIED OUT ON BEHALF OF THE RESEARCH COMMITTEE OF THE BRITISH TUBERCULOSIS ASSOCIATION AND OF THE ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

THE REPORT HAS BEEN PREPARED ON BEHALF OF THE JOINT SUB-COMMITTEE REPRESENTING THE TWO BODIES

BY

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THIS report analyzes the results obtained in a controlled trial of streptomycin and para-aminosalicylic acid in the treatment of endometrial tuberculosis. The investigation was started in July, 1950 and ended in December, 1952. It was conducted by a Joint Sub-Committee representing the Royal College of Obstetricians and Gynaecologists and the Research Committee of the British Tuberculosis Association. Patients were treated at Birmingham, Edinburgh, Exeter, Glasgow, London and Oxford. A preliminary report on this trial has already been published in this *Journal* (Sutherland, 1954). The trial is now completed, and the purpose of this communication is to present the final results in the form of a brief supplementary report.

* The following took part in the investigation:

Dr. A. M. Sutherland (*Chairman*).
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Mr. R. A. Brews.
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PRESENT SERIES

The total number of cases originally admitted to the trial was 126, but for various reasons it was found necessary to exclude 13 of these from the present analysis. Of the 126 patients admitted to the trial between July, 1950 and December, 1952, 78 were from Glasgow, 16 from Oxford, 11 from Birmingham, 9 from London, 6 from Edinburgh, and 6 from Exeter.

Clinical Features

The findings in this paper are based on a study of the remaining 113 cases. The principal complaints are shown in Table I.

Bacteriology

Bacteriological proof was sought in almost every case, and a positive result was obtained in 87 instances. In most of these, an attempt was made to type the organism. This was successful in 67 cases, 63 being of the human type and the remaining 4 of the bovine variety. An attempt was made to obtain bacteriological confirmation from the vast majority of the endometrial specimens obtained. In the whole trial 417 endometrial specimens were examined, and bacteriological confirmation was sought in 392 of these.

Sensitivity of the organism to streptomycin was tested in 68 instances (60 strains were isolated initially and 8 later in the trial). The assessment of sensitivity was carried out according to the recommendations of the

TABLE I
Presenting Symptoms of Patients in Trial

	Total Patients	Infertility	Pain	Bleeding	Amenorrhoea	Vaginal Discharge	None	No Record
Treated	61	27	13	8	5	0	6	2
Control	52	26	10	5	5	2	3	1
Total	113	53	23	13	10	2	9	3

Medical Research Council Sub-Committee (1948). A standard culture H37RV was obtained from the Medical Research Council laboratory. This was found to be sensitive to 0·25 μg. of streptomycin. In assessing the tested organisms, they were considered to be sensitive if their growth was inhibited by less than 1 μg. of streptomycin. Of the 68 cases tested for sensitivity, 62 were found to be streptomycin-sensitive.

In the remaining 6, a streptomycin-resistant organism was found (the resistance ratio was 16 in one case and 8 in the other 5). In 3 instances, the streptomycin-resistant organism was obtained at the initial examination, and no further positive cultures were obtained after treatment. None of these patients, as far as is known, had received any anti-tuberculous chemotherapy before entering the trial. In the fourth case, a control, the organism obtained from the first endometrial specimen was streptomycin-sensitive, but a subsequent specimen obtained at the end of the control year was streptomycin-resistant. This patient also gave no history of previous treatment of any kind. The other two streptomycin-resistant organisms were obtained after treatment with streptomycin, the first after 84 g. and the second after 25 g. (this case had a resistance ratio of 16); treatment in the latter case had to be discontinued because of a toxic reaction.

MANAGEMENT

The cases were initially allocated at random to either "Treatment" or "Control" groups. The cases in the "Treatment" group were given 1 gramme of the calcium chloride complex of streptomycin daily by intramuscular injection for 84 consecutive days, and 3 grammes of PAS (sodium salt) 4 times daily by mouth over the same period. Progress was assessed by regular endometrial biopsy during the follow-up year, and by full curettage under anaesthesia at the end of the year. There were 61 patients in the "Treatment" group, and treatment had to be discontinued before the end of the course in 4 of these because of toxic drug reactions.

There were 52 patients in the "Control" group. No treatment was carried out, and the patients were kept under observation during a period of one year. During this time no less than 11 required immediate treatment because of clinical deterioration, usually a flare-up of the tuberculous condition in the pelvis. These 11 patients were removed from the trial and were treated; they were not subsequently included with the "Treatment" group. The cases withdrawn from the trial for various reasons are shown in Table II and the results in the "Treatment" and "Control" groups are compared in Table III.

RELATIONSHIP BETWEEN RESULTS AND BACTERIOLOGY

Table IV shows the results according to the nature of the diagnosis, and it will be seen that the figures obtained for the bacteriologically-proved cases are in reasonable agreement with those for the whole series.

RESULTS OF TREATMENT IN RELATION TO SYMPTOMATOLOGY

No treated patient complaining of infertility became pregnant, although one patient complaining mainly of abdominal pain did so and went successfully to term, with delivery of a live child. The results in relation to the remaining complaints were mainly satisfactory, and most patients reported relief of their symptoms.

TABLE II
Withdrawals from Trial

	Total Cases	Exclusions				Spread of Disease		Total Remaining
		Faulty Records	*Myco. tub.* Bacilluria	Pulmonary Tuberculosis	Drug Reaction	Pelvic	Extra-Pelvic	
Treatment ..	66	4	0	1	4	0	0	57
Control ..	60	5	3	0	0	9	2	41
Total ..	126	9	3	1	4	9	2	98

TABLE III
Results One Year After Entry to Trial

	Total Patients Followed Up for One Year	Endometrium Positive		Endometrium Negative		Percentage Negative		
		Bacteriological	Histological Only	Bacteriological	Histological Only	Bacteriological	Histological Only	Total
Treated ..	43	5	—	37	1	86	2	88
Control ..	33	14	11	7	1	21	3	34

TABLE IV
Results One Year After Entry to Trial According to Nature of Diagnosis

	Diagnosis	Total Patients Followed Up for One Year	Endometrium Positive	Endometrium Negative
Treated	Bacteriological	34	5 H. 0 B. 5	29
	Histological only	9	0	9
Control	Bacteriological	25	21 H. 7 B. 14	4
	Histological only	8	4 H. 4 B. 0	4

H=Histological diagnosis only.
B=Bacteriological diagnosis.

DISCUSSION

It is apparent that the results obtained in the treatment of endometrial tuberculosis by streptomycin and PAS for 12 weeks are much better than those observed in the controls as judged on the basis of a 12-months follow-up. The occurrence of toxic manifestations in 4 patients during treatment is disturbing, although in no case were there any permanent ill-effects.

As far as the control cases are concerned, although a number did apparently heal without treatment, the results obtained show that one is not now justified in withholding treatment from any patient with proved tuberculosis of the

endometrium. The main reasons for this conclusion are the fact that the majority of cases in the "Control" group remained positive on follow-up and the fact that a substantial number showed clinical deterioration in the course of the trial and required immediate treatment.

Further trials have been in progress since May, 1953, in which streptomycin and PAS are being compared with streptomycin and isoniazid and with isoniazid and PAS, and different durations of treatment are being contrasted. While the present results are satisfactory in view of the short period of treatment, it is probable that longer periods comparable with those used currently in other forms of tuberculosis will prove even more effective.

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MERALGIA PARAESTHETICA

With Reference to Its Occurrence in Pregnancy

BY

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MERALGIA paraesthetica, first described by Bernhardt in 1878, is characterized by pain, numbness and paraesthesia in the distribution of the lateral cutaneous nerve of the thigh. It may occur as part of a polyneuritis or as a result of a clearly defined pathological process in the vicinity of the nerve, such as osteoarthritis of the lumbar spine or an inflammatory condition in the iliac fossa. However, interest has been directed to its occurrence as an isolated mononeuritis and it is this type of case with which this paper is concerned.

Very few reports on the occurrence of this condition in association with pregnancy have been published. Horvath (1899) and Price (1909) each reported a case in which the syndrome recurred in successive pregnancies. Musser and Sailer (1900) reported 2 cases occurring in pregnancy, Lee (1936) reported one further case and Ecker and Woltman (1938) included 2 pregnant women in their series of 150 cases of meralgia paraesthetica collected from the records of the Mayo Clinic. More recently, Peterson (1952) has reported one further case. Both King (1941) and Schneck (1947) consider that meralgia paraesthetica occurs more frequently than it is diagnosed.

Three further cases occurring in pregnancy are reported here, because it is thought that it may be more common in pregnant women than is generally realized, offering a positive diagnosis for some of the "pressure pains" and neuritides presented by the antenatal patient.

AETIOLOGY

The lateral cutaneous nerve of the thigh is wholly sensory and arises from the posterior roots of the 2nd and 3rd lumbar nerves. It emerges from the lateral border of the psoas major at the iliac crest and runs across the iliacus, beneath the fascia iliaca, towards the anterior superior iliac spine, where it enters the thigh by passing medial to the spine and deep to the inguinal ligament. The anterior branch pierces the deep fascia 9 cm. below the inguinal ligament to become superficial and supply the skin of the antero-lateral aspect of the thigh down to the knee. The smaller posterior branch supplies the skin over the greater trochanter and the neighbouring part of the thigh.

Occasionally, the lateral cutaneous nerve enters the thigh by passing through, or even lateral to, the origin of the sartorius (Stookey, 1928).

In its passage from the iliac fossa to the thigh the nerve describes a sharp bend at the apex of which is the inguinal ligament. In a certain proportion of people the nerve does not pass under the inguinal ligament but runs through a canal formed by an anterior and posterior fasciculus of the ligament. It is believed that meralgia paraesthetica is particularly liable to occur in these people, since extension of the hip joint or a lumbar lordosis, by stretching the nerve, exposes it to trauma by the posterior fasciculus.

Contractions of those muscles of the anterior abdominal wall, which are attached to the lateral end of the inguinal ligament, may also traumatize the nerve by a shutter-like action as shown by Mack (1946).

Obesity plays a part in the aetiology of meralgia paraesthetica by altering posture and possibly by pressure or traction of panniculi on the nerve. The average weight of 90 per cent of the patients in Ecker and Woltman's series was 79·5 Kg. (12 stones 7 pounds) and 11 patients

had reported a rapid increase in weight before the onset of symptoms. In one case in their series the aetiological factor was apparently ascites. These authors attribute its onset in pregnancy to increased tension in the abdominal fasciae; they do not appear to have considered the possible aetiological significance of exaggerated lumbar lordosis.

Pathology

In the literature, both macroscopic and microscopic reports on the nerve differ widely. Only cases treated surgically by resection of part of the nerve or those coming to autopsy can be studied microscopically. King reports 5 cases, showing definite neurological signs, treated by resection of a segment of the nerve. In 4 cases the nerve was normal, but the fifth showed marked degeneration with disappearance of axis cylinders and this was the only case presenting cutaneous anaesthesia. In Mack's case the nerve was macroscopically thinned, but in an autopsy case quoted by Corlette (1944) the nerve, which had been traumatized by the iliac crest, presented a spindle-shaped swelling and microscopically showed neuritis and perineuritis with dissolution of the nerve fibres. In isolated cases a number of other gross pathological features have been reported.

Clinical Features

The condition is commoner in the male than the female, the proportion being about 3 : 1, and is generally unilateral. Symptoms and signs are referred to the cutaneous distribution of the lateral cutaneous nerve on the antero-lateral aspect of the thigh. The first symptom is numbness, which is followed by stinging pain and paraesthesia in the area. These symptoms are brought on by standing and by any action involving extension of the hip joint. They are relieved by sitting or lying down. Very occasionally trophic lesions appear.

In mild or early cases there may be no objective sensory loss, but in cases of moderate severity there is diminution of light touch, pain and temperature perception in the area. In severe cases there is a central zone of anaesthesia. Deep sensation is constantly maintained (Ecker and Woltman, 1938).

In the majority of cases the characteristic pain can be produced by passive extension of the hip joint.

Diagnosis

The characteristic features should make the diagnosis obvious, but the possibility of the cause of the neuritis being elsewhere than at the nerve's entry into the thigh must not be overlooked.

Case Reports

Case 1

V.U., a primigravida, aged 31, at a routine visit to the antenatal clinic at the 30th week of pregnancy, complained of attacks of "pins and needles", numbness and some pain over the lateral aspect of the right thigh. These symptoms had been present for 2 weeks.

Pregnancy had been uneventful otherwise and general physical examination revealed no abnormality. The Wassermann reaction was negative. Her height was 5 feet 3 inches (160 cm.) and her weight 11 stones 4 pounds (72 Kg.). The weight gain since the 14th week of pregnancy was 17 pounds 8 ounces (8 Kg.).

No definite sensory loss could be established in the right thigh, but, in view of the characteristic symptoms, meralgia paraesthetica was diagnosed. The patient was reassured and a mild analgesic prescribed, which appeared to relieve her symptoms.

Delivery was spontaneous at term, after which the condition cleared up completely.

Case 2

E.B., aged 28, was seen at the 36th week of her second pregnancy, when she complained of pain and tingling over the antero-lateral aspect of the right thigh. Her previous pregnancy and delivery had been uneventful. Symptoms had been present for one month and were aggravated by standing and walking, but pain was never severe.

Pregnancy had been uneventful otherwise and general physical examination revealed no abnormality. The Wassermann reaction was negative. Her height was 5 feet 5 inches (165 cm.) and her weight 10 stones 4 pounds (67·3 Kg.). The weight gain since the 13th week of pregnancy was 17 pounds (7·7 Kg.).

Over a large area on the antero-lateral aspect of the right thigh the sensations of touch and temperature were diminished, but those of pain and deep pressure were normal. The stretch reflexes were normal and there was no loss of power. Passive extension of the right hip-joint caused pain and tingling in the area. Extension of the left hip-joint was painless. A radiograph of the lumbar spine showed no relevant pathology.

She was advised to wear a corset and a mild analgesic was prescribed. A week later she reported slight diminution of pain, but at 39 weeks pain was continuous and was severe enough to keep her awake at night.

Labour was induced by artificial rupture of the membranes 5 days before term and spontaneous delivery

FIG. 1

Case 2. The area of anaesthesia on the right thigh one month after delivery.

of a healthy male child weighing 7 pounds 15 ounces (3·6 Kg.) occurred on the following day. The total duration of labour was 4 hours and 5 minutes. Pain in the leg disappeared on the second day of the puerperium, but complete anaesthesia was demonstrated in the affected area.

Seven weeks post-partum the area of anaesthesia was unchanged. Three months after delivery the area of anaesthesia was still unchanged (Fig. 1), but at the end of 6 months slight sensation was demonstrated in the peripheral part of the area. She complained of tingling and numbness, but no pain.

Case 3

M.F., a primigravida, aged 24, at her first visit to the antenatal clinic, at the 10th week of pregnancy, complained of burning pain and numbness on the outer aspect of the left thigh. These symptoms had been present since the eighth week of pregnancy. She was otherwise perfectly well. The Wassermann reaction was negative. Her height was 5 feet 4½ inches (164 cm.) and weight was 10 stones 1 pound (64 Kg.). At 18 weeks, when the symptoms were unchanged, calcium lactate was prescribed. At 22 weeks the pain was increasing in intensity and was aggravated by standing and walking. Her weight was then 10 stones 12 pounds (69 Kg.). An area of anaesthesia measuring 11 inches by 6 inches was found on the antero-lateral aspect of the left thigh. Surrounding this area was a 2-inch strip in which sensory perception was diminished. Deep sensation was normal. Severe pain in the area was evoked by passive extension of the left hip-joint. There was no loss of power in the limb and the reflexes were normal. X-ray examination of the lumbar spine revealed no abnormality.

The patient was admitted to hospital and put to bed. She was fairly comfortable in bed, but pain returned when she got up. One week later, 20 ml. of 1 per cent procaine was injected at a point 1 cm. medial to the anterior superior iliac spine. This was followed by diminution of pain for a few hours only.

Three days later, under general anaesthesia, the lateral cutaneous nerve was exposed at its point of entry into the thigh by Professor Aird. The nerve was seen to enter the thigh by passing through the inguinal ligament. It exhibited a fusiform swelling for a distance of several inches immediately distal to the inguinal ligament. The posterior fasciculus of the ligament was divided and the nerve freed from the surrounding connective tissue. The wound was closed in layers without drainage. Operation was followed by complete relief from pain until wound sepsis occurred one week later. This cleared up rapidly and the wound had healed completely by the end of the second post-operative week. Pain on standing and walking, which had recurred coincidentally with the wound infection, persisted, but was never at any time severe. The area of anaesthesia did not alter.

Spontaneous delivery of a healthy male child, weighing 8 pounds 5 ounces (3·7 Kg.), followed a normal labour of 24-hours duration at term. All pain disappeared after delivery, but anaesthesia persisted.

She became pregnant again 18 months later and soon began to complain of burning pain on standing and walking. Pain persisted throughout pregnancy, but was much less severe than it had been pre-operatively in her first pregnancy. It disappeared completely after spontaneous delivery at term of a healthy male child, weighing 9 pounds 8 ounces (4·3 Kg.), but she still complains of numbness. As she left the London area before her second pregnancy began, there has been no opportunity to examine her personally.

Discussion

The three cases of meralgia paraesthetica reported here all presented symptoms for the first time during pregnancy. This suggests that the anatomical and physiological concomitants of pregnancy may have some bearing on its aetiology. The enlarging uterus itself cannot exert direct pressure on the lateral cutaneous nerve, but the consequent tension on the muscles and fasciae of the abdominal wall may have this effect. The latter was considered by Ecker and Woltman to be the main aetiological factor in the pregnant woman. In cases where the nerve passes through a canal in the inguinal ligament the tension on the adjacent muscle attachments must tend to expose the nerve to trauma from the posterior fasciculus of the ligament.

Lumbar lordosis tends to stretch the nerve and again trauma will be most likely to occur in cases where it passes through the inguinal ligament.

Apart from abdominal swelling, fluid retention by the tissues increases the tension of the abdominal wall. This factor is difficult to assess except in so far as weight gain during pregnancy bears some relation to fluid retention as well as to increase in size of the uterus and its contents and obesity. In the first and second cases reported here, gain in weight was within normal limits. In the third case it was above normal in the first and second trimesters and this patient developed symptoms at the 8th week, whereas the others did not do so until the 28th and 32nd week respectively. None of the patients showed abnormal mobility at the symphysis pubis. It might be conjectured that laxity of the iliofemoral ligament, due to hormonal influence in early pregnancy, could have altered the posture and accelerated the onset of the condition in this case. In the case reported by Price, symptoms came on at the 8th week in two successive pregnancies and one of Musser and Sailer's patients started to complain of symptoms at the 2nd

month. In Lee's case, symptoms commenced at the 36th week in her first pregnancy, but recurred at an early stage of a subsequent pregnancy. Where sufficient data are given, other cases are seen to have started in the third trimester.

In the second case reported here, the complete absence of symptoms in the previous pregnancy is interesting. Presumably some alteration in posture, perhaps due to the previous pregnancy, determined the onset of symptoms in the second pregnancy. A similar sequence may have occurred in the case reported by Lee and referred to above; symptoms only appeared at the 36th week of the first pregnancy, but came on in a severe form early in the third. Unfortunately, the intervening pregnancy receives no mention.

The choice of treatment depends upon the severity of the symptoms and the stage of pregnancy at which the condition is diagnosed. Mild cases with slight pain and minimal sensory disturbance need only explanation and reassurance. Attention should be paid to obesity and faulty posture and the patient should be advised to avoid long periods of standing.

In more severe cases, pain may be so intense that the patient is unable to carry out her normal household duties. If she is put to bed, the pain usually disappears, only to recur as soon as she gets up. Induction of premature labour, when the foetus is sufficiently mature, should be seriously considered if pain is severe. Induction of labour was carried out a few days before term in Case 2 of the present series, but one wonders whether permanent anaesthesia might have been avoided by earlier induction.

Severe cases occurring in early pregnancy present a more difficult problem. Lee (1936) reports that pain was so severe in his case that pregnancy had to be terminated. Rather than adopt this course, one should attempt surgical cure of the condition itself. The nerve is exposed through a transverse incision over the lateral end of the inguinal ligament and its anatomy is inspected. If it emerges between an anterior and a posterior fasciculus of the inguinal ligament, the posterior fasciculus should be divided and the nerve freed from any constricting fascial bands. In Case 3 of the present series, pain was relieved by this procedure, but returned with the onset of wound sepsis, persisted in a mild form until delivery and recurred in a subsequent pregnancy. This nerve is probably surrounded by dense fibrosis, but the pressure upon it appears to have been partially relieved.

If the nerve emerges beneath the inguinal ligament a different procedure must be adopted. Pain may be relieved by division or resection of the nerve but an area of permanent anaesthesia will be produced. The latter is, perhaps, not a matter of great importance, but an ideal method is one which will both relieve pain and restore normal sensation. Such a method may be the transplantation operation described by Lee (1941) in which the nerve is placed in a slot cut in the iliac crest and surrounded by fat pedicles. He reported complete relief of symptoms in 2 cases following this operation.

Summary

Three cases of meralgia paraesthetica in pregnancy are presented.

The aetiology of the condition is discussed and the clinical features and treatment briefly summarized.

Acknowledgment

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TRAUMATIC MATERNAL BIRTH PALSY

BY

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INTRODUCTION

WHILE the birth palsies which affect the newborn child are well recognized, it is not generally known that during parturition the mother may suffer damage to certain of the nerve trunks in the pelvis, resulting in a birth palsy affecting her lower limbs. The condition may vary from a transient paresis to a widespread paralysis of certain groups of muscles in one or both legs and occasionally there may be some permanent damage to the muscles involved.

The condition has been described in the literature under a number of titles; Windscheid (1899) wrote about neuritis puerperalis, Tillman (1935) about traumatic neuritis of the puerperium. Beattie (1933) and O'Connell (1944) termed it maternal obstetrical paralysis while Mills (1945) termed it peroneal palsy, this being a reference to the constant involvement of the muscles supplied by the peroneal branch of the sciatic nerve.

The incidence of the lesion has been estimated at 1 in 2,000 deliveries but we have found it impossible to arrive at any definite figures. Many of the milder cases recover rapidly and are not reported; one of our patients was referred from a postnatal clinic where she had made a casual reference to a weakness in one of her feet. She had not considered the weakness of any moment and would certainly not have sought treatment for it. During the past 9 years we have seen 9 patients in orthopaedic clinics where they had been referred for advice and treatment. Apart from the one mentioned above, all had been sent by general practitioners, 4 after their return home from the hospitals where they had been delivered. Details of one further case have been received from another unit and the mother of a physiotherapist who knew of our interest in the condition came to consult us as she had suffered from the complaint following the birth of her daughter 19 years previously. The total of cases reviewed in this publication is thus 11.

In the past many theories have been put forward to account for the paralysis. Romberg (1853) disagreed with those obstetricians who attributed it to compression of the sciatic nerves in the pelvis. Lambrinudi (1925) was of the opinion that during delivery sacral rotation was sufficient in these cases to exert traction on the lumbo-sacral cord, one of the tautest nerves in the body which follows a short course over the pelvic brim. He opposed the theory that the nerve was compressed at the pelvic brim on the grounds that it should be protected by the sacral prominence from pressure of the foetal head. Barns (1943) could not agree with Lambrinudi's view; he believed that any lesion due to sacral rotation would be bilateral and bilateral lesions were rare. O'Connell, after a study of 4 cases, came to the conclusion that the lesion was caused by prolapse of an intervertebral disc. Cole (1946) made a radiological study of his cases and concluded that all had pelves which were characteristic, the features being shortening of the posterior ilium with flattening of the sacral promontory and shallow anterior concavities of the sacral alae. Chalmers (1949) was able to find 142 cases recorded in the literature up to that time and to these he added another 4; he believed that 2 of these were due to compression, 1 to sacral rotation and 1 to disc protrusion and concluded that different mechanisms could operate in the production of the lesion. Other writers, notably Beattie (1933) and

Kleinberg (1937), have attributed the paralysis to the use of instruments at delivery.

We favour the view that, under certain circumstances, the lumbo-sacral cord may be damaged by direct pressure of the foetal head during labour. We have carried out some experimental work in an attempt to support our opinion and it will be dealt with in the discussion which follows a brief account of each case.

(1) M.L., aged 39 years, reported to the department 5 weeks after the birth of her second baby. About the third or fourth day after the delivery she noticed a numbness and weakness of her right foot. Following the birth of her first baby three years before she had had a similar experience. On that occasion the right foot had been weak and numb for 6 weeks, but had recovered spontaneously without treatment. With her second child the weakness was more marked and as there was no evidence of recovery in 5 weeks she had been sent to hospital. Examination revealed a partial drop foot with only a flicker of contraction in the extensors of the toes and foot; the peronei were contracting weakly. The patient made a complete recovery after 5 months physiotherapy and splints were worn for 2 months. Both deliveries were spontaneous; the weight of the first child was not recorded but the second weighed eight and a half pounds. The mother was four feet ten inches in height.

(2) Mrs. A.J., aged 32 years, had a second child, a male weighing 10 pounds, which was delivered after labour lasting 6 hours. The delivery was completed with the use of instruments and general anaesthesia. She was seen two days later at the request of her practitioner on account of paralysis of both legs. Examination revealed bilateral drop foot; the muscles supplied by both peroneal nerves were involved and there was anaesthesia over L 4–5 segments. There was also weakness of the muscles of both buttocks. She was admitted to hospital where drop foot splints were applied. A radiograph of the pelvis (Fig. 1) showed a dislocation at the symphysis pubis. During her six weeks stay in hospital physiotherapy was given and she was discharged wearing bilateral calipers to attend the out-patient department. Eighteen months passed before she had sufficient return of power to discard the calipers and 6 years after there is still weakness of the extensors of the toes, the extensor hallucis longus remaining paralyzed on the left side. This patient was five feet in height.

(3) Mrs. A.S., a primipara, was delivered of a female child weighing eight and a half pounds. Labour lasted ten and a half hours and delivery was spontaneous. She was seen in the out-patient clinic 13 days after delivery with a right drop foot. There was complete loss of power of the tibialis anticus, and only a flicker of contraction in the extensors of the toes and peronei. Sensory loss was present over L 4–5 segments. A caliper with a drop foot stop was fitted and she attended the out-patient physiotherapy department. Within 3 months there was sufficient recovery to discard the caliper. It was nearly a year before full power had been recovered but 3 years later there was still an area of hypo-aesthesia over the dorsum of the foot and leg. The patient stated that for a few weeks before delivery she had experienced a discomfort in the leg. The patient's height was barely five feet.

(4) Mrs. J.S., a primipara aged 29 years, was sent to the out-patient clinic 6 months after the delivery of her child on account of a right drop foot. The delivery had been a difficult one necessitating the use of instruments. When she got up on the tenth day she noticed that she had no control over her right foot. On account of the health of the child and domestic circumstances six months elapsed before she reported. The muscles in the anterior compartment of the leg were all functioning though weakly, there was no true anaesthesia, but a patch of hypo-aesthesia was present over the characteristic area. Recovery was complete in 2 months during which time she attended the physiotherapy department. The baby weighed eight pounds at birth and the mother was under five feet in height.

(5) Mrs. J.B. noticed a weakness and numbness in the left leg when she returned home after the delivery of her second child in hospital. Examination showed diminished power in the extensors of the left foot and an area of hypo-aesthesia over the dorsum of the foot and outer side of the leg. The weakness was not considered sufficient to require treatment and spontaneous recovery took place in about 2 months. Delivery was unassisted, labour lasted about 7 hours, the baby weighed 8 pounds 10 ounces, and the mother's height was five feet and half an inch.

(6) Mrs. M.McG., who delivered her second child spontaneously after a labour lasting six and a half hours, noticed a weakness in her right foot on the following day. Three weeks later she was referred to the out-patient clinic, where she was found to have a partial drop foot. There was complete paralysis of the tibialis anticus, and considerable diminution of power in the extensors of the toes and the peronei. She was fitted with a caliper and returned home, being unable to attend for treatment. Six months later she had complete recovery apart from a degree of paraesthesia in the dorsum of the foot. The baby weighed 8 pounds 1 ounce, and the mother's height was five feet.

(7) Mrs. M.M., aged 24 years, had her second baby in hospital. Labour was induced at the 39th week and lasted 6 hours. The delivery was spontaneous but, while in the labour room, during one of her pains she felt her right foot and leg go numb. She returned home ten days after delivery and was not seen by us until three months later. At that time there was weakness of the tibialis anticus, extensors of the toes and peronei and an area of hypo-aesthesia over the dorsum of the foot and leg. She felt that there had been some improvement before we saw her, and after three months attendance at the physiotherapy department there was complete recovery of both muscle power and sensation. At birth the baby weighed 8 pounds 14 ounces; the mother was four feet eleven inches in height.

(8) Mrs. M.L. was referred from a postnatal clinic 6

months after the birth of her first baby, on account of weakness of her left leg and foot. Her labour was prolonged and had to be completed by instrumental delivery. During one of her pains, some time before she was anaesthetized for forceps delivery, she felt her left leg go numb and she was unable to move the leg or the foot. She returned home with her baby not having made any mention of her foot while in hospital. During a routine visit to a postnatal clinic she mentioned it to the doctor in charge who referred her to our clinic. Examination revealed a mild degree of wasting and weakness of the extensors of the foot and ankle, the peronei were functioning normally, and there was the usual area of hypo-aesthesia over the L 4–5 distribution. She attended the physiotherapy department twice weekly and had made a full recovery when seen two months later. The baby was 8 pounds at birth and the patient was five feet in height.

(9) Mrs. M.K., aged 26 years, was seen in May, 1955. Her first baby was born in hospital 3 months previously and she herself had been very ill after the delivery. When she returned home 4 weeks after the birth she felt her left leg was dead and she could hardly walk. It was now much better but still felt weak and numb. On examination there was weakness of the dorsiflexors of the foot and ankle, and an area of diminished sensation over the outer side of the foot and calf of the left leg. She is still attending the physiotherapy department. The baby was 7 pounds at birth and the mother, a slightly built woman, was four feet eleven inches in height.

(10) Mrs. M.H., a primipara, aged 25 years, had a very difficult labour lasting 50 hours. The child was stillborn. When she had recovered from her difficult labour she complained of numbness and loss of power in her left leg; there was no history of acute pain in the leg during labour. Seen two days after the delivery which had been spontaneous she had absence of dorsiflexion and inversion of the foot; there was loss of sensation above the lateral malleolus. She was allowed home shortly afterwards with a splint. On her next visit to the clinic a week later it was found that the muscle weakness was much more extensive, the glutei were weak, there was no power in the peronei and the hamstrings were not as strong as the normal side. She was fitted with a caliper and drop foot stop and attended for electrical stimulation and exercises. Eight months later the patient had completely recovered. No record was made of the weight of the child which was stillborn. The mother was reported as being just over five feet in height.

(11) Mrs. M. came to see us because of our interest in this subject. Her only child was born when she was 39 years of age. Towards the end of the pregnancy she developed eclampsia and was very ill; the delivery was instrumental and her baby weighed 7½ pounds. Following her confinement she had weakness of her left leg and foot which she said were quite useless. At that time her practitioner thought it might be a white leg and she was kept in bed for several months but eventually was allowed up wearing a caliper. She had treatment from a masseur and it was one year before she recovered full use of the leg. The patient's height was four feet and eleven inches.

Clinical Picture

From a study of our cases the clinical picture may be summarized. Premonitory symptoms have been reported by other writers but were present in only one patient in this series. She was a primipara and we believe this fact is relevant when symptoms are present before delivery. Following the delivery a degree of nerve involvement becomes apparent, varying from a very slight paresis and paraesthesia up to complete paralysis and anaesthesia in the distribution mainly of the peroneal branch of the sciatic nerve. When the degree of nerve involvement is extensive the glutei and the calf muscles are affected. Chalmers quoted a case in which the femoral nerve was involved but we have not been able to find any weakness in the femoral distribution in our cases. The paralysis is not usually noticed by the mother until several days after the delivery, but two of our patients were aware of its onset during their labour pains. Most of the mothers in this group seemed to regard the weakness of the foot as a necessary evil associated with childbirth and struggled along under a considerable handicap until the child was thriving before reporting to hospital.

If in hospital the mother may overlook or disregard the weakness in the excitement of the delivery and in her anxiety to get home. Once home and having resumed her household duties the weakness of the leg and foot becomes more apparent, she trips over the carpet and eventually is sent to an orthopaedic or neurological clinic. Either leg may be involved, occasionally both, and the condition may recur in later deliveries.

In this series the parity of the patient does not appear to be a significant aetiological factor, but it is the opinion of one of us (J.T.B.) that in obstetric practice premonitory symptoms suggestive of nerve pressure are comparatively common in the primigravid patient during the last four weeks of pregnancy. This we believe is due to the attempt of the foetal head to engage in the pelvic brim during that period.

Prognosis

The prognosis on the whole is good. Mild cases recover within 2 to 3 months but more severe lesions may take a year. One of our cases has a permanent paralysis affecting the extensor

of the great toe and a partial weakness of the long extensor of the toes, which while a handicap in some respects does not prevent her performing her household duties.

Treatment

The treatment in all our cases has been carried out in the physiotherapy department and consisted of electrical stimulation, massage, graduated movements and exercises. In the more severe cases calipers were fitted and night splints supplied. It was usually possible to discard the caliper once active muscle power had returned, but our severe bilateral case had to wear them for eighteen months.

Discussion

The set pattern of the muscle weakness and sensory upset seemed to us to indicate a common mechanism of injury and a lesion peculiar to labour and delivery. We could not visualize a number of different conditions resulting in the same constant lesion. Six cases were delivered spontaneously and 5 had an instrumental delivery and of these one was aware of the onset of the paralysis before being prepared for the application of the forceps. This evidence makes it appear unlikely that instrumental delivery is a direct aetiological factor.

Lambrinudi's theory of sacral rotation appeared unlikely. Like Barns we felt that in such a case the lesion would be bilateral. In fracture dislocation of the pelvis even with wide displacement of the sacro-iliac joint nerve involvement is not a feature. Urist (1953) reported one case under the title "Obstetric Fracture Dislocation of Pelvis with Injury to Lumbosacral Trunk and First Sacral Nerve Root". A woman, aged 37, spontaneously delivered herself of a female child weighing 10 pounds 10 ounces after a 2-hour labour. One and a half hours after the onset of labour she had a sudden sharp pain, heard a crack, and felt something give in the left sacro-iliac region. Twenty-four hours later when she attempted to get up the pain recurred and she had tingling coldness and lack of sensation in the left leg and weakness of the ankle. This history is typical of our group and we feel that this was in reality a traumatic maternal birth palsy.

Repeated examinations failed to reveal any evidence of disc lesion in any of our patients. Radiographs taken over a number of years showed none of the changes one would expect to find, such as narrowing of the affected disc space or lipping of the adjacent vertebrae. Weakness of the anterior tibial group of muscles with sensory changes in the affected segment is quite common in disc lesions of the lumbar spine, but complete drop foot is relatively uncommon and in such cases one would expect to find some of the other classical signs of lumbar disc lesions such as backache, sciatica, limitation of movement of the lumbar spine, and limited straight leg raising on the affected side, but we could find no evidence of these. We have treated a number of pregnant women with acute disc lesions of the lumbar spine and have found them to differ in no way from the classical picture.

Experimental Investigation

Both the superior and the inferior gluteal nerves, and the lateral peroneal nerve, which supply the muscles affected, receive fibres from the lumbosacral cord. This cord passes over the pelvic brim in the region of the sacro-iliac joint where it is joined by the first sacral nerve. At the brim it lies on the bone which may actually be grooved by it, and here it is deep to the common iliac artery. As it turns over the brim it is deep to the internal iliac artery, the psoas lying to its lateral side. The position and course of this cord were determined by examination of subjects at autopsy. A rubber tube of similar dimensions filled with mercury was used to replace the nerve in a female pelvis (Fig. 2a). A foetal skull flexed as in labour was next introduced into the pelvis, and pressure brought to bear on it to try to compress the cord. Figure 3 shows that such compression is possible and that the sacrum does not prevent the foetal head from coming into contact with the nerve.

Conclusion

All our patients were women of small stature with relatively large babies, resulting in a degree of cephalo-pelvic disproportion not sufficient to obstruct labour but of sufficient degree to cause the foetal head to compress the structures at the pelvic brim as it passed through. X-ray

FIG. 1

Radiograph showing separation at the symphysis which occurred in Case 2.

FIG. 2a

Female pelvis in which the lumbo-sacral trunk was replaced by a rubber tube filled with mercury.

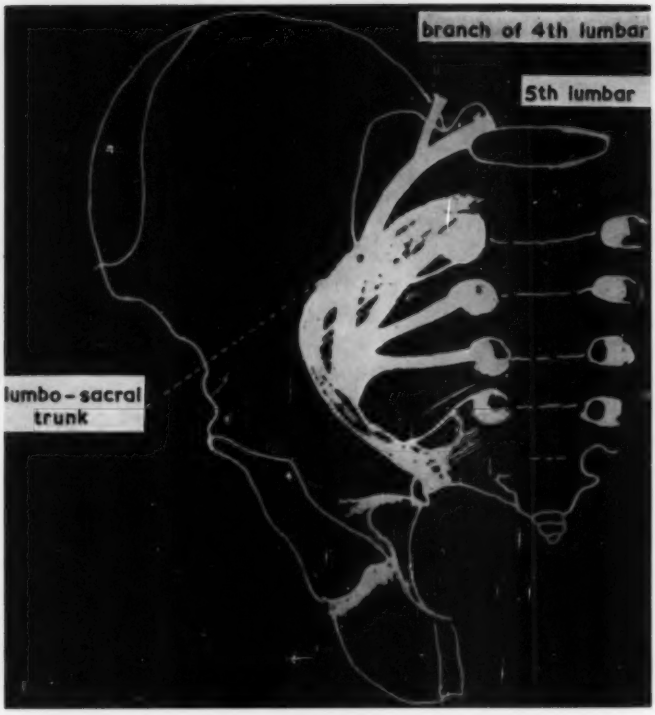

FIG. 2b

Diagram to illustrate the lumbo-sacral cord and the point at which it is subjected to pressure as it crosses the pelvic brim.

(*a*) (*b*)

FIG. 3

Foetal head inserted into the pelvis shown in Fig. 2a, and made to press against the sacrum and pelvic wall. The antero-posterior (*a*) and lateral (*b*) radiographs show a break in the mercury where the foetal head is compressing the tube against the pelvic wall.

examination of the pelves of these women revealed no gross bony variations from the normal gynaecoid form but the tendency to justo-minor deformity was noted. That cephalo-pelvic disproportion existed was shown by the fact that a number of the deliveries were difficult and in 2 cases there was a separation of the symphysis pubis. Presentation in every case was vertex and it is likely that the nerve damage occurred on the side occupied by the occipital pole of the foetal head when the lesion was unilateral but we have insufficient knowledge of the deliveries of these patients to prove this.

The question of prevention was studied at some length but it seemed impossible of solution. If prevention of the lesion is possible it will result from the knowledge that lumbo-sacral nerve trauma may occur in small women during the course of labour if the foetus is large.

In cases where a degree of cephalo-pelvic disproportion is suspected and where, in the course of labour, pain is complained of in the distribution of the lumbo-sacral cord, one may be well advised to terminate the labour by Caesarean section. To apply forceps in such circumstances would probably increase rather than lessen the risk of nerve trauma.

All our cases except one recovered completely but the period of disability may be prolonged and in severe cases there may be a degree of permanent weakness. Many women after delivery complain of indefinite symptoms referable to one or other leg and no objective signs are found on examination. We believe that minor degrees of compression of the lumbo-sacral cord are responsible for these symptoms.

Summary

(1) The literature on birth palsy is reviewed and the various theories as to its causation are discussed.

(2) The clinical course, treatment and prognosis are discussed with reference to eleven cases.

(3) Experimental evidence is given for our belief that the lesion is due to compression of the lumbo-sacral cord as it crosses the pelvic brim.

Addendum

Since this paper was forwarded we have seen one further case of drop foot. The patient, a young woman of 21 years of age, had her baby on 2nd February, 1956. Instruments had to be used and the baby was stillborn. We have no note of the child's weight. Following the delivery the mother had a typical drop foot on the right side. She was seen by the neurosurgeons who after examination agreed that she was a case of traumatic maternal birth palsy and referred her to us. She was fitted with a caliper and physiotherapy commenced. She became pregnant again and was delivered by Caesarean section on 20th February, 1957. At the operation we took pains to examine the lumbo-sacral cord and blood vessels on the right side of the pelvis. There was no evidence of any definite pathological lesion from her previous delivery but it was noted that the cord and blood vessels were easily palpable and in a position where they could quite easily be subjected to trauma by the foetal head. She has made no progress in so far as recovery of the drop foot is concerned. She is 4 feet 11 inches in height.

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TREATMENT OF TRICHOMONAS VAGINITIS WITH TERRAMYCIN VAGINAL PESSARIES

BY

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INTRODUCTION

IT was thought possible to improve the results of treatment of trichomonas vaginitis by using Terramycin vaginal pessaries in the belief that local absorption would eradicate the parasite from the cervical glands and the vaginal rugae, and so diminish the incidence of relapse.

SELECTION OF PATIENTS AND DIAGNOSIS

The series comprises 23 patients in whom a clinical diagnosis of trichomonas vaginitis was confirmed by microscopic examination of the vaginal exudate; patients with concomitant vaginal thrush, Neisserian infection or who were pregnant were excluded.

TREATMENT

Each patient was instructed to wash her hands and insert a 100 mg. pessary of Terramycin high up into the vagina night and morning for 40 consecutive days and nights, during which time sexual intercourse and douching were forbidden, and treatment was continued throughout the menstrual period.

FOLLOW-UP

All patients were seen two, three, six months and one year after commencement of treatment, with the exception of one who defaulted at 2 months, one who defaulted at 3 months and one who defaulted at 6 months. All patients were examined clinically and a fresh preparation of the vaginal transudate was examined microscopically.

RESULTS

The cures at 2 months number 12. Four of these patients relapsed at 3 months but no fresh relapses were seen thereafter.

COMMENTS

The ages of the patients range from 16 to 54. One had had a total hysterectomy and unilateral salpingo-oöphorectomy at the age of 29 and 1 had been sterilized. Of the 23 patients 16 were married and 7 were single. The group fertility appears sub-normal and the incidence of menstrual irregularity was high. No significance could be attached to toilet habits, the use of public baths or the position of the uterus.

CONCLUSION

The use of Terramycin pessaries in the treatment of trichomonas vaginitis gives no better results than methods of treatment in current use.

I am grateful to Pfizer Ltd. for the supply of Terramycin vaginal pessaries.

ACUTE PANCREATITIS SIMULATING INTRAPELVIC BLEEDING IN PREGNANCY

BY

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THE case history given below is considered of sufficient interest to report since acute pancreatitis in pregnancy is a rare condition. The problem was unusual since the patient's condition suggested the possible occurrence of intrapelvic haemorrhage.

CASE REPORT

Mrs. L.F., a 4-gravida, aged 23 years, was admitted into hospital on 1st April, 1956, as an emergency case. She had always experienced good health and her previous confinements had been normal. There was, however, a 4-months history of indigestion, commencing in December, 1955, and during this time a marked intolerance to fatty foods had developed. The onset of the last menstrual period was 24th February, 1956.

Sudden pain in the upper abdomen which radiated into the back occurred 48 hours prior to admission. The pain, which was intermittent but not very severe, remained in the epigastric region for only a few hours and then the abdominal distribution became more generalized. No persistent back pain was felt. For 24 hours before entering hospital there was left shoulder tip pain and the abdominal pain was maximum in the left loin and left iliac fossa.

Severe nausea with occasional vomiting was present from the onset of the condition. No vaginal bleeding was observed at any time.

On examination the patient was found to be pale and slightly shocked. The blood pressure was 100/60. There was a slight pyrexia of 99° F. and the pulse rate was 100. The abdominal tenderness was generalized but most marked in the left loin and left iliac fossa. No distension and no abdominal wall rigidity were found. The Grey Turner (1920) or Cullen (1918) phenomena were not apparent.

A pelvic examination revealed a slightly enlarged anteverted uterus and movement of the cervix caused severe pain. There was marked pelvic tenderness, which was maximum in the left fornix. No apparent abnormality of the uterine appendages or any pelvic mass could be felt.

The clinical findings were suggestive but not typical of intrapelvic bleeding having occurred possibly from a ruptured tubal pregnancy. It was decided to explore the abdomen.

A laparotomy was performed through a left subumbilical paramedian incision. The peritoneal cavity contained brownish-coloured free fluid. The uterine enlargement corresponded to an 8-weeks gestation and the uterine appendages were normal. The pancreas was easily palpable and apparently oedematous. The omentum showed multiple small areas of fat necrosis and a small calculus could be felt in the gall-bladder.

The diagnosis of acute pancreatitis was made and the abdomen closed with drainage of the peritoneal cavity.

For 96 hours after operation continuous intra-gastric suction was maintained and intravenous fluids given. Prophylactic chemotherapy in the form of streptomycin and penicillin was administered. The convalescence was satisfactory except for a deep thrombophlebitis of the left leg which rapidly cleared up.

The maximum serum amylase was 1,600 Somogyi units/100 ml. the day after operation. A Hogben test carried out some days later was positive.

Unfortunately the patient was readmitted into hospital when 12-weeks pregnant on account of an abortion and it was necessary to evacuate the uterus.

DISCUSSION

The term acute pancreatitis is used in a wide sense and may describe a condition where the inflammatory involvement of the gland may be only slight or one of fulminating necrosis. The causation of pancreatitis is uncertain and, although numerous causes have been put forward, the predisposing factors are yet incompletely understood. The relationship to pregnancy is seen in the fact that 39 (73 per cent) of the 53 cases collected from the literature by Langmade and Edmondson (1951) occurred in the puerperium. There is in many cases evidence of associated gall-bladder disease. MacKenzie (1954) found that 50 per cent of his female patients with acute pancreatitis had concomitant biliary lesions. Siler and Wulsin (1950), in a clinical study of 98 cases of acute pancreatitis, reported a 34·2 per cent incidence of gall-bladder disease as shown by X-ray

examination, by operation and at post-mortem. There were stones in the gall-bladder or common bile duct in 29·7 per cent of the series. Four only had any recent history of pregnancy and in these the acute condition occurred in the puerperium; 3 of them had associated gall-bladder disease.

Aird (1949) makes the statement that "the diagnosis of acute pancreatitis can often be made with some confidence if the possibility of the condition is kept in mind".

In over half of the cases (53·2 per cent) reviewed by Siler and Wulsin (1950) the pain originated in the epigastrium but it may be prominent in other locations and thus is often confused with that of other conditions. Nausea and vomiting with occasional epigastric discomfort are common in pregnancy particularly during the early months. Langmade and Edmondson (1951) record one fatal case of acute pancreatitis complicating pregnancy where a diagnosis of hyperemesis gravidarum was made.

One of the most useful diagnostic tests is the serum amylase estimation and it might have been helpful if it had been carried out before operation in the case described. The serum amylase may be increased in conditions other than acute pancreatitis. MacKenzie (1954) found that the elevation of the serum amylase might be transient and last only 24 hours. It does appear, however, to be the most useful laboratory test for diagnostic purposes. In some cases an exploratory laparotomy is the only method of making a diagnosis.

Summary

A case of acute pancreatitis which simulated intrapelvic bleeding in early pregnancy is described.

There is frequently an associated lesion in the biliary system in cases of acute pancreatitis.

I wish to thank Dr. W. J. Clancy, City General Hospital, Sheffield, for permission to publish this case.

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CARCINOMA *IN SITU* OF THE ENDOMETRIUM

BY

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MOST pathologists have made at some time a confident diagnosis of carcinoma of the endometrium on a specimen obtained by curettage only to find, when the uterus has been removed, that there is no trace of malignant tissue in the specimen. Such a finding leads to much heart-searching on the part of the pathologist and his staff and occasions great anxiety to the gynaecologist; the other specimens received on the same day are checked, fresh blocks are cut from the extirpated uterus and a feeling of uneasiness prevails throughout the department. The case here reported illustrates the condition of such a uterus before the diagnostic biopsy.

CASE HISTORY (35415)

The patient, a single woman aged 33 years, was admitted because of excessive menstrual loss, generalized abdominal pain and a persistent feeling that her bladder was full. On examination she was found to have an enlarged, retroverted uterus and to have some pain on pressure in the posterior fornix. Her menses had been irregular and heavy since the menarche at the age of 12 years and had been accompanied by severe pain. Ten years before she had undergone dilatation of the cervix for dysmenorrhoea and 7 years previously had been admitted to the Women's Hospital, Liverpool for dilatation of the cervix, curettage and progesterone implantation. On the latter occasion the endometrium showed abnormal proliferative activity of the type usually associated with endocrine dysfunction, that is, there was some thickening of the gland epithelium with stratification of the nuclei and moderate dilatation of the glands. There was no evidence of malignancy. Review of this section confirms that there was at the time no evidence of malignancy.

At operation, 7th February, 1956, 20 days after the start of the last menstrual period, the uterus was found to be enlarged and its configuration distorted by several small fibroids; there was an area of roughening on its posterior aspect which was thought to be a patch of endometriosis. In view of the endometriosis and the number of fibroids total hysterectomy was carried out; the ovaries were conserved to avoid the distressing withdrawal symptoms of oöphorectomy in a young woman.

The specimen received in the laboratory consisted of a uterus grossly distorted by several fibroids, the largest of which was 7 cm. in diameter, and the proximal ends of both Fallopian tubes. There was an area of roughness on the posterior surface of the body of the uterus just above the peritoneal reflexion. On opening the uterus a yellow plaque 7 mm. in diameter and 2 mm. thick was found in the endometrium on the posterior wall of the uterine cavity; the plaque was firm in consistency and well demarcated from the surrounding endometrium.

Histological examination showed the cervix to be normal; the myometrium was normal except for a number of benign fibroids which showed some hyaline change. The endometrium was thin and there was no evidence of secretory activity in the glands, the epithelium of which showed some stratification. The histological picture was similar to that seen in the previous specimen and is typical of endocrine dysfunction (Fig. 1). The yellow plaque consisted of closely packed hyperplastic glands, some of which showed papillary projections into the lumina. The gland cells were large and eosinophilic, the nuclei were vesicular with some condensation of the chromatin and mitoses were infrequent (Figs. 2 and 3). The atypical glands were confined to the endometrium, there was no invasion of the myometrium and there was a clear distinction between the plaque of abnormal glands and the remaining endometrium. The area of roughening on the back of the uterus showed endometriosis; the glands were of the same type as those in the greater part of the

endometrium. No glands of the type seen in the solitary yellow plaque were seen in the area of endometriosis nor in any of the parametrial tissues.

Discussion

The isolated plaque of atypical endometrium totally different from that seen in the rest of the endometrium would, if seen in "curettings", be regarded without hesitation as indicative of malignancy and hysterectomy would subsequently be carried out. In its present context it is revealed as a pre-invasive carcinoma, carcinoma *in situ* of the endometrium. This lesion is of the type formerly called "adenoma malignum". This term is to be avoided as an adenoma, which is a benign tumour, should not be qualified by an adjective implying malignancy; the condition is malignant although at a very early stage.

Carcinoma *in situ* is, by definition, a malignant condition in which the only abnormalities are the morphological changes in the cells themselves and in their arrangement in the tissue; evidence of infiltration is absent. This problem has been reviewed recently by Fennell and Castleman (1955) who point out that the lesions of pre-invasive cancer can be found in many parts of the body in which they were previously unrecognized. In many sites overt cancer may co-exist side by side with carcinoma *in situ* which may make a bridge between the malignant and normal tissues. It is probable that in nearly all cases the malignant process is fully established at this stage and that progression to overt malignancy with invasion and metastasis is inevitable and inexorable. A small number of cases however have been seen in which a diagnosis of carcinoma *in situ* has been made but no major operative procedure has been carried out and overt cancer has not developed. These may be cases in which the cancerous process has been arrested by the body defence mechanism (Des Ligneris, 1940) but it is also possible that the whole of the lesion has been removed at the initial diagnostic biopsy (Peightal, Brandes, Crawford and Dakin, 1955).

The concept of carcinoma *in situ* of the endometrium is clouded by the extreme degree of atypical proliferation which may be seen in this situation. Carcinoma of the endometrium is ordinarily a disease of post-menopausal women who have never borne children and many workers believe that there is a gradual transition through the various types of endometrial hyperplasia to carcinoma and that it is impossible to define with certainty the borderline between atypical hyperplasia and malignancy (Novak, 1947; Novak and Rutledge, 1948). Hertig and Sommers (1949) studied a series of cases of carcinoma of the body of the uterus in which previous endometrial biopsies had been performed; these authors found that in only 12 of 47 biopsies taken from 1 to 23 years before the diagnosis of carcinoma of the endometrium was made was there a normal cyclical endometrium. Two of the remaining biopsies on re-examination showed invasive carcinoma which had been missed on first examination, 2 showed changes which they considered on the borderline between carcinoma *in situ* and invasive carcinoma and 6 showed carcinoma *in situ*. The remainder of the specimens showed some degree of endometrial hyperplasia with loss of the normal cyclical pattern. In addition these writers reported the frequent occurrence of other endocrine disorders, diabetes, sterility and obesity in their total series of over 300 cases of carcinoma of the endometrium and suggested that some form of endocrine dysfunction may be at any rate a predisposing factor in carcinoma of the endometrium. These workers did, however, recognize a definite histological entity of carcinoma *in situ* (Hertig, Sommers and Bengloff, 1949). They described 64 cases of carcinoma *in situ* of the endometrium which they had collected over a period of 15 years and found a typical histological picture which was distinct from that seen in non-malignant endometrial hyperplasia. The glands of the endometrium were packed closely together with a minimal amount of stroma separating them, the gland cells were large with abundant clear cytoplasm and irregular nuclei which showed a loose chromatin network with coarse aggregations of chromatin. In none of their cases was the lesion visible to the naked eye.

This association of carcinoma of the endometrium with endocrine dysfunction is especially seen when the condition occurs in a younger

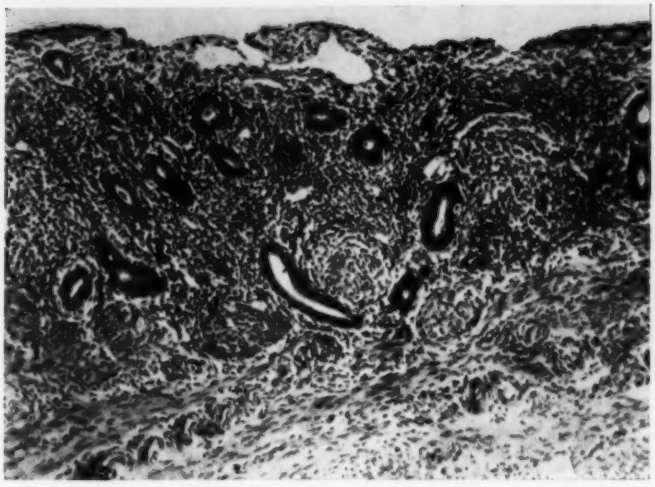

FIG. 1

Endometrium showing absence of secretory activity and stratification of the nuclei of the gland cells. H. & E. × 125.

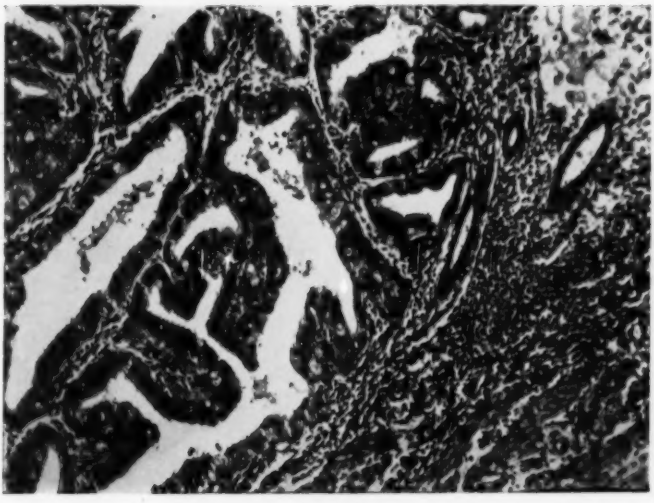

FIG. 2

Endometrium showing the junction between the uninvolved endometrium on the right and the tumour on the left. The tumour shows the closely packed glands with papillary projections in the lumina. H. & E. × 125.

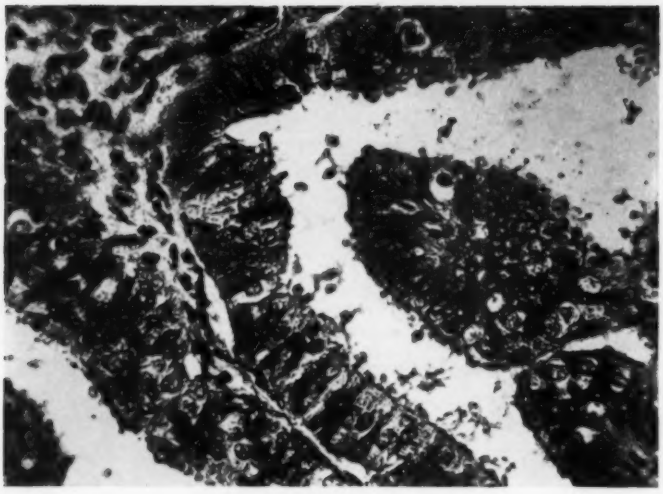

FIG. 3

High power view of the tumour tissue showing the large cells with clear cytoplasm and the irregular nuclei. H. & E. × 400.

patient. Such patients are usually suffering from a state of chronic endocrine imbalance manifested by irregular and often excessive menstruation and often by the presence of fibroids in the myometrium (Sommers, Hertig and Bengloff, 1949; Dockerty, Lovelady and Foust, 1951).

The present case presented with a clinical history similar to those reported by Sommers *et al.* and by Dockerty *et al.*; she had suffered from menstrual irregularity all her life and was found at operation to have multiple fibroids in her uterus. The lesion in the endometrium, which showed no evidence of invasion, was histologically similar to those reported by Hertig, Sommers and Bengloff although it was readily detected by naked eye examination. Had the uterus been curetted at this time and the whole of the lesion removed, which might well have been the case, a diagnosis of carcinoma of the body of the uterus would undoubtedly have been made, the uterus would have been removed and searched for evidence of tumour without success.

The presence of a localized malignant lesion in the endometrium in the presence of atypical hyperplasia suggests that endocrine dysfunction is not the whole cause of the disease and that there is some additional factor involved. This is in accord with the view of Fahlund and Broders (1946) who examined the uninvolved endometrium in a series of cases of endometrial carcinoma and found that there was no gradual change from hyperplastic endometrium to carcinoma. Similar views were expressed by Geist, Walter and Salmon (1941) who found that there was no increase in the incidence of carcinoma following oestrogen therapy although such therapy is a cause of endometrial hyperplasia, and by Rewell and Towers (1956) who examined the mucosa of the Fallopian tubes in a series of 50 cases of carcinoma of the endometrium and found no evidence of hyperoestrinism.

Summary

A case of carcinoma *in situ* of the endometrium of a woman of 33 has been reported. She had suffered throughout her life from menstrual irregularity and dysmenorrhoea. The macroscopic and microscopic appearances of the uterus showed that there had been a chronic state of endocrine dysfunction but that there was a tumour which was sharply demarcated from the rest of the endometrium.

The concept of carcinoma *in situ* has been briefly reviewed and it has been pointed out that this type of lesion in the uterus may present, to the pathologist, as a curetting on which a confident diagnosis of carcinoma is made but that search of the extirpated uterus reveals no trace of tumour. The prognosis in such a case is, of course, excellent.

The origin of carcinoma of the endometrium by gradual metamorphosis from a state of endometrial hyperplasia has been briefly considered. This case is adduced in support of the thesis that there must be, in addition to the abnormal endometrium, some additional cause for the development of carcinoma.

I am indebted to Sir Arthur A. Gemmell, *M.C., T.D.*, for permission to report this case, who was admitted to hospital under his care, and for his encouragement.

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A CASE OF CHORIONEPITHELIOMA

BY

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AND

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THE literature contains many reports of cases of chorionepithelioma diagnosed at varying times after normal confinement. In the case reported it is apparent, in retrospect, that evidence of the disease existed during the course of a supposedly normal pregnancy. An X-ray examination of the chest was carried out at the 33rd week of pregnancy and revealed pulmonary metastases, the origin of which was unknown. Re-X-ray 2 weeks later showed the deposits to be more extensive. The diagnosis was finally made 5 weeks after this, on the 26th puerperal day, when biopsy of a secondary vaginal deposit revealed chorionepithelioma.

The patient, aged 23 years, was admitted to the Christchurch Hospital on 22nd April, 1954 in the 33rd week of her first pregnancy. The last menstrual period began on 5th September, 1953, and the pregnancy had been uneventful until the night of admission, when the patient was injured in a car accident. Investigation included X-ray examination of the chest and pelvis. The latter showed fractures of the superior pubic rami and the ischio-pubic rami on both sides, but without displacement. In the chest film the ribs were intact, but there was shadowing in the right mid-zone, the significance of which was not understood at this time (Fig. 1).

During the next 14 days uterine contractions occurred, but labour did not ensue. However, the patient complained of abdominal pain of greater severity than that to be expected, either from the injury, or the nature of the uterine contractions. On the 13th May the X-ray examinations were repeated, and, in the case of the chest, it was apparent that more extensive shadowing now occupied the right mid and lower zones and the left lower zone.

Labour began on 15th May, 1954 at the 36th week of pregnancy, and spontaneous delivery of a normal male infant weighing 5 pounds 4 ounces occurred the next day in the St. Helens Obstetrical Hospital. The third stage of labour was uneventful, and the placenta appeared normal to the naked eye.

The puerperium was complicated by fever, abdominal pain and distension, and repeated vaginal bleeding. On the 21st puerperal day a bluish purple tumour about 1 inch in diameter was seen on the anterior vaginal wall a short distance above the external urinary meatus (Fig. 2). The pathologist's report on the biopsy of this stated: "The sections show much blood clot with masses of fibrin, often infiltrated by polymorphs and large masses of trophoblastic tissue. This last consists of syncytial masses and Langhans' cells, the former predominating. The nuclei of both layers vary in size and shape, are hyperchromatic, with some giant forms, but mitoses are rare. Much of the tissue is necrotic. No vaginal wall structures are recognizable but the site of origin of this material and its structure indicate chorionepithelioma."

X-ray examination of the chest was repeated on 18th June, 1954 when there were numerous discrete shadows throughout both lung fields, an appearance consistent with that of multiple blood-borne secondary deposits (Fig. 3). Comparison of these films with those taken on 22nd April at the 33rd week of pregnancy, and 3 weeks before delivery, confirmed that lung metastases were in fact present at that date.

FIG. 2
Vaginal metastases of chorionepithelioma,

FIG. 1
X-ray of the chest on 22nd April, 1954.

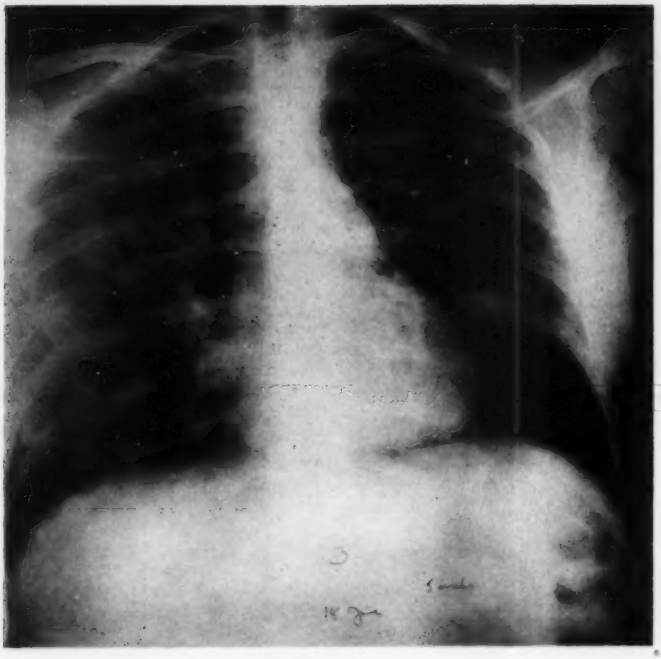

FIG. 3
X-ray of the chest on 18th June, 1954.

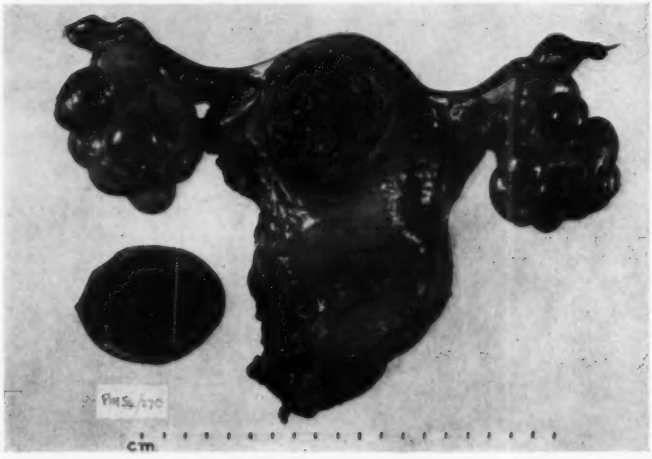

FIG. 4
Uterus showing chorionepithelioma with ovaries containing lutein cysts.

The Hogben test on 20th June was positive in a dilution of 1/1,000.

The patient's general condition was now poor and considered unsuitable for surgery. Treatment was by intra-uterine and vaginal radium, deep X-ray therapy to the chest, and by repeated blood transfusion. The vaginal deposit resolved completely but the pulmonary lesions became more extensive until death occurred, after haemoptysis, on 8th August, 1954.

Unfortunately permission for full post-mortem examination was not obtained, the uterus and appendages only being examined. The pathologist reported as follows: "There is a smooth rounded swelling projecting from the anterior surface of the uterine body. The serous coat is intact. The Fallopian tubes appear normal but both ovaries are grossly enlarged by clusters of cysts, generally filled by greenish watery fluid but in some cases containing altered blood. The vaginal mucosa and cervix are deeply congested, but their epithelium is intact. A firm haemorrhagic mass fills and distends the uterine cavity and arises from the anterior uterine wall, which is the seat of a tumour approximately six inches in diameter. This tumour invades and replaces the myometrium, and at its periphery small islands almost reach the serous coat (Fig. 4).

"Microscopically there is deep infiltration of the muscle wall by chorionic cells of both Langhans' and syncytial type, showing markedly irregular and hyperchromatic nuclei. There is frequent invasion of vascular spaces by the tumour tissue. Apart from the actively proliferating and infiltrating peripheral zone, the tumour is haemorrhagic and necrotic. The ovarian cysts are lined by luteinized cells with some nuclear irregularity. No tumour tissue can be identified in the vagina."

Discussion

Had it not been for the coincidence of a car accident necessitating X-ray examination of the chest, the chorionepithelioma in this case would have been regarded as arising after the confinement.

Pulmonary metastases are common in this disease and occurred in 55 per cent of Novak's 74 proved cases. The vagina was the next most common site for secondary deposits, being involved in 16 per cent (Novak and Seah, 1954). Comparable figures given by Brews (1939) were 37·5 per cent and 29 per cent respectively. The disappearance of the vaginal deposit after treatment in this case is in keeping with the well-known radiosensitivity of this tumour, although spontaneous disappearance of metastases has been recorded.

This case fulfils Novak's criteria for diagnosis of chorionepithelioma (Novak and Seah, 1954):

(1) The presence of large islands or fields of trophoblastic cells, usually a mingling of both syncytial and Langhans' elements.
(2) Necrosis of muscle.
(3) Haemorrhage.
(4) Mitoses rare although hyperchromatosis common.
(5) Chorionic villi not seen.

Summary

A case of chorionepithelioma is described, diagnosed 4 weeks after a normal delivery. Vaginal and pulmonary metastases were present. Pulmonary metastases were demonstrated radiologically 3 weeks before delivery, but the nature of the primary lesion was not known until 7 weeks later. The disease was rapidly fatal.

Acknowledgment

We wish to thank Dr. W. Mark Brown, Senior Gynaecologist to the Christchurch Hospital, and Dr. D. T. Stewart, Director of Pathology, for help with this case.

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THE TRANSVERSE DIMENSION OF THE UTERUS DURING THE PUERPERIUM

BY

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THE transverse measurement of the puerperal uterus has received very little attention in textbooks and professional literature, and its clinical significance seems never to have been appreciated. Observation of this measurement, however, is a matter of some value in clinical obstetrics and should be more frequently used as a method of estimating the progress of involution. For this purpose I believe that it is superior to the time-honoured method of observing the height of the fundus, especially since some factors may increase the height of the uterus and give an erroneous impression of uterine size. These factors are chiefly the condition of the bladder and recto-sigmoid and the strength of the pelvic floor muscles. Some obstetricians and teaching centres have abandoned recording the descent of the uterus as a curve on the temperature chart as being unreliable. In estimating uterine size from day to day the lower pole cannot be palpated whereas both sides can, and to those who have used this measurement a distinct and uniform change is evident, departures from which can be detected distinctly.

In a large series of measurements made on the first day post-partum the uterus shows an average width of 6½ inches and this measurement is quite constant, whereas measurements on the sixth day show considerable variation. These measurements vary from as low as 2½ inches to an occasional case where the width remains 5 inches or more, the average of 3½ inches being taken to represent the normal.

It is admitted of course that exact measurement of actual uterine size is not possible through the intervening abdominal wall. In any given patient, however, the projection of the uterine borders through the abdominal wall, especially when consecutive observations are made by the same examiner, gives a very true measurement. In about 5 per cent of cases the uterine width cannot be measured because of such causes as obesity, bowel loops in front of uterus, etc., but these also interfere with observations of the fundal height. The tonus of the abdominal muscles occasionally interferes with palpation of the lateral borders, but can usually be overcome by postural relaxation of the abdominal wall.

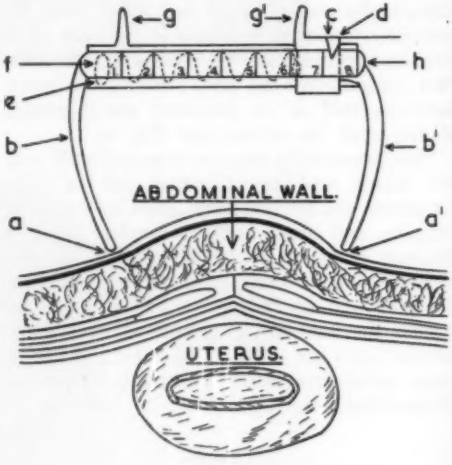

FIG. 1

Cross-sectional view to show uterometer in use. The points a and a^1 are placed on the uterine borders. The arm b^1 and the sleeve c, with indicator d, are in one piece and move freely along the tube e connected with the arm b. Inside the tube is a spring f which is compressed when the finger grips g and g^1 are approximated. This allows an accurate adjustment to the uterine width and a direct reading on the scale.

Besides its use as a measure of involution the uterine width merits observation during the 3rd stage of labour and shortly after it as it provides an early warning of some possible complications such as concealed haemorrhage due to uterine atony or hour-glass contraction, etc.

No special instruments are necessary in order to utilize the information obtained from this examination. In clinical obstetrics the daily palpation of the lateral borders between the finger-tips gives an estimate which is sufficient. In other cases where actual measurement is desired the widest point is palpated and, with the skin held stationary, the borders are marked and the measurement is taken. As the uterus is freely mobile in a side-to-side plane, the palpation and marking must be done simultaneously for both borders. It is also possible to measure with a tape between the tips of the palpating finger and thumb without marking the skin.

An instrument for taking this measurement may vary widely in design. Figure 1 shows one such instrument which is both simple and practical.

Although an experienced obstetrician can estimate involution quite accurately and is not easily misled by unusual positions of the uterus, nevertheless for teaching purposes and exact estimations the transverse measurement will be found of value and, I feel, deserves to be more widely used.

ACKNOWLEDGMENTS

I tender my sincere thanks to Professors R. W. Johnstone and R. J. Kellar of Edinburgh for their constructive criticism, and also to Dr. F. B. Macdonald for his help in preparing this paper.

A CASE OF CO-EXISTING HYDATIDIFORM MOLE AND LIVING CHILD

BY

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MRS. J.A., aged 22 years, first attended The London Hospital in September, 1954, because of 8-weeks amenorrhoea. The expected date of the confinement was 26th April, 1955.

PAST OBSTETRICAL HISTORY

In 1950, when unmarried, she was delivered of a full-term healthy infant. The child's father was an Englishman.

In 1953, now married to a Nigerian, she aborted a hydatidiform mole at the Mile End Hospital. The mole was confirmed histologically. It occurred after 6 months of amenorrhoea and was followed by curettage. Five months later the Aschheim-Zondek test was negative.

PRESENT PREGNANCY

In early November, 1954, after 14 weeks of amenorrhoea, the Aschheim-Zondek test was positive undiluted and negative in a dilution of 1 in 25. The patient remained well until she reached the 32nd week. She was then admitted to hospital because of the sudden onset of severe pre-eclampsia, the blood pressure reading 160/95, and the urine contained two-thirds volume of albumen. After 2 weeks of treatment the toxaemia had only slightly improved. By now, according to her dates, she was 34-weeks pregnant, and the fundal height corresponded. On the 15th March labour commenced spontaneously and 24 hours later a living female infant was born. The third stage was completed uneventfully.

The child's birth weight was 4 pounds 2 ounces (Fig. 1). She cried readily at birth. On examination the abdomen was found to be grossly distended the girth measuring 14½ inches. The nature of the cystic abdominal swelling was rather uncertain until a laparotomy disclosed a multicystic liver which filled the abdominal cavity and extended to the pelvic brim. The ovaries and other viscera appeared to be normal.

The infant lived for 10 months during which time the abdomen did not decrease in size. Shortly before death she weighed 19 pounds. She died of pneumonia, and at post-mortem the liver was found to be polycystic with a one-inch perimeter of normal hepatic tissue.

The placenta weighed 4 pounds (Fig. 2). It was 2 inches thick and 9½ inches in diameter. Macroscopically about three-quarters of the placenta seemed to have undergone hydatidiform degeneration. The histologists reported on a biopsy as "hydatidiform mole, enlarged degenerative avascular villi with evidence of only mild trophoblastic activity, together with numerous normal looking villi. No evidence of chorionepithelioma."

THE PUERPERIUM

Twenty-four hours after delivery the Aschheim-Zondek was positive, but negative when diluted to 1 in 12. Four weeks later the neat test was negative, and remained so until the next pregnancy.

Two days after delivery the patient was examined under anaesthesia. The ovaries were found to be normal in size, and some small pieces of placental tissue were curetted from the uterine cavity. These curettings were reported to contain "degenerate and inflamed decidual tissue together with occasional hydropic degenerate villi".

By the tenth day all signs of pre-eclampsia had disappeared.

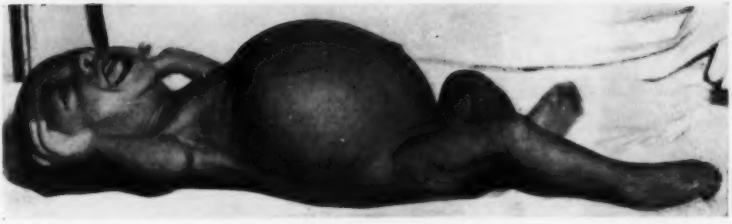

FIG. 1
Female infant with an enlarged abdomen due to a polycystic liver.

FIG. 2
Hydatidiform placenta.

Subsequent Obstetrical History

In September, 1955, the patient had a spontaneous abortion after 8 weeks of amenorrhoea. There was no evidence of hydatidiform degeneration in the curettings.

In July, 1956, the patient was delivered of a normally developed female infant weighing 5 pounds 11 ounces. The pregnancy had been uneventful until at the 36th week placenta praevia was diagnosed. The child was delivered by Caesarean section and during the operation the patient's ovaries were seen to be normal in size and appearance. Histologically the placenta showed no sign of hydatidiform mole.

Discussion

The birth of a living infant with hydatidiform changes in its placenta is a rare occurrence. About 14 cases have been reported, but some of these are not well authenticated. The description of the placenta of one case of nearly 30 years ago was typical of what we now know to be haemolytic disease of the newborn. Other cases were not clear as to whether or not the moles were associated with multiple pregnancies.

It is of interest that this patient conceived her first living child by an Englishman, and all the subsequent, including the two molar pregnancies, by her Nigerian husband. The reduced fertility is related to the husband but it is doubtful if this factor is a cause of the hydatidiform change. There is no evidence to show that this disease is commoner among Nigerians, or, for that matter, in mixed marriages (Lawson, 1956; Hertig, 1956).

Recurrence of a hydatidiform mole is rare, its incidence being about 1 per cent (Brews, 1939). Hertig (1956) knows of 2 patients each of whom aborted 3 successive moles. He suggests that once this anomaly has recurred it is likely to do so again. This view is not substantiated by the presented case.

The pregnancies of the reported cases have all been complicated by severe pre-eclampsia and only one, rather surprisingly, had some bleeding during the early months. Most of them terminated in spontaneous premature labour.

Of 9 infants born with hydatidiform moles, 4 had congenital abnormalities, 2 were found to be normal, and there were no comments on the other 3. Only one of these abnormalities was incompatible with life. The high incidence of neonatal deaths has probably been connected with prematurity. It is interesting that all the babies, where the sex has been noted, were females. Unfortunately their ovaries were not described.

A review of many of these unusual cases has shown that about 75 per cent of each placenta had undergone hydatidiform degeneration. Not one of them had shown a malignant change.

Summary

A case of a co-existing hydatidiform mole and living female infant is presented. A review of the literature has been made.

Acknowledgments

I wish to thank Mr. Victor Lack for permission to publish this case; and also to thank Mr. Lack and Mr. Alan Brews for their comments.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

AT the Meeting of Council held in the College House on Saturday, 25th May, 1957 with the President, Sir Charles Read in the Chair, the following were elected to the Council to fill statutory vacancies:

As representatives of the **Fellows:**

LONDON	William Charles Wallace Nixon.
ENGLAND AND WALES (excluding London)	Francis Edward Stabler.
SCOTLAND	Thomas Nicol MacGregor.
NORTHERN IRELAND AND EIRE	Charles Horner Greer Macafee.

As representatives of the **Members:**

LONDON	Thomas Loftus Townshend Lewis.
SCOTLAND	Robin Murdoch.

The following was admitted to the **Honorary Fellowship:**

Sir Russell Brain, Bt., M.A., D.M., F.R.C.P.

The following were admitted to the **Fellowship:**

Paul Cowell Barkla.
Trevor Samuel Montague Barnett.
Francis Arthur Bellingham.
Norman Brandon Capon.
Daphne Wai Chan Chun.
Alexander Culiner.
William Davies Cunningham.
James Paton Orr Erskine.
Mary Evans.
William Rodgers Foote.
Fergus Duncan Johnston.
Kenneth Turville Macfarlane.
Thomas Alistair Macfarlane.
George Burwell Maughan.
Daw Yin May.
Wilfrid George Mills.
Kripananda Mitra.
John Gregory O'Donoghue.
Henry Edwin Pellew.
Percy Peltz.
Don Abraham Ranasinghe.
William Joseph Rawlings.
Ronald McKenzie Rome.
Douglas Walter Sparling.
Dorothy Marian Stewart.
James Walker.
John Forrester Brown Wyper.

The following were admitted to the **Membership:**

Douglas Crowe Aird.
George Bryan Batchelor.
Ralph Anthony Timothy Boland.
Graeme Dickinson Desmond Cable.
Mahomed Ismail Cassimjee.
John Samuel William Chambers.
Probhat Kumar Choudhuri.
Charles Alan Blake Clemetson.
Kenneth Ivor Digwood.
Ammud Freier.
William John Garrett.
William Gault.
William Gavin.
Ivan Goldman.
Christoffel Jacobus Goosen.
Bernard Kirsch.
Margaret Amy Lakeman.
Edwin William Lillie.
Hamish Heathcote McCrostie.
John George Markus.
Andrew Edward Bertie Matthews.
Terence Thomas Erskine Michael.
Antony Bruce Miller.
Arun Kumar Mitra.
Jessie Mary Buchanan Muirhead.
Allan Clarke Cullen Pinion.

Lawrence John Rice.
Ray Richards.
Thomas Joseph Ryan.
Grahame Julian Witherington Stump.
Sarosh Meher Thanevala.
Kenneth Francis Gilmore Wilson.
Robert Yule.

List of Candidates who have been awarded the **Diploma in Obstetrics:**

Donald Andrew Aitken.
Robert Winfred Allin.
Alexander Arnold Allison.
Andrew Armstrong.
Geoffrey Arthur Evelyn Baker.
Vijayaratnam Balachandran.
Amarendra Banerjee.
Arthur Frank Barrett.
Richard William Beard.
Felicity Margaret Bedford.
Kailash Bhalla.
John Terence Binless.
Philip Metcalfe Binns.
Geoffrey Colin Bird.
Sybil Dora Bonuini.
Walter Michael Stewart Boyd.
Ronald Thomson Boyle.
Paul Vincent Briffa.
Keith Granville Buckler.
Mary Elizabeth Budleigh.
Michael Francis Digby Burton.
Sheelah Caldwell.
Donald John Craig Cameron.
John James Camp.
Hamish Argyll Campbell.
Peter John Summers Cannon.
Gerald Caplan.
John Malcolm Carr.
Bryan Ranger Thomas Carroll.
Leela Mary Chacko.
John Edward Charlewood.
Ronald Robert Charlwood.
Helen Clarke.
Barrie John Clayton-Payne.
Derek John Cliffe.
David Treasure Cousins.
Alan Fergus Crowley.
George Harper Charlton Daley.
Surendra Nath Das.
David John Davies.
Edna Lynette Davies.
Walford Farr Thomas Davies.
Pauline Mary Dean.
Hermanus Van Zyl de Klerk.
Leslie Peter de Souza.
Raymond Dingley.
Pamela Mary Dodson.
Marion Ramsey Haddow Donald.
Alan Malcolm Donaldson.
Brian Gerard Dooley.
Ronald Basil Dorofaeff.
Brian John Drake.
Richard Edmund Dreaper.
Florence Mary Duckenfield.
Geoffrey Henry Hewlett Dwyer.
Judith Margarete Edmundson.
Philip Arthur Edmund Edmundson.
Philip Earle Elwood.
Michael Entwisle.
John Earl Evans.
Lewis William Sturt Eyears.
Edith Faierman.
David Fairbairn.
Frederick George Feinstein.
Elizabeth Ann Fisher.
Anthony Francis Floyd.
Beryl Margaret Foley.
Hugh Kelson Ford.
Eric Jeffrey Heywood Foster.
James Frame.
Andrew Thomas Radburne Fuller.
Richard Gardner.
Ethel Florence Edwards Gelber.
Srasht Kumari Ghai.
Saroj Kumar Ghosh.
Harrison Raymond Gibson.
Benoy Bhusan Giri.
Stanley Lester Goodman.
Colin Michael Green.
Everel Catharine Green.
William Francis Griffith.
Peter Griffiths.
David Simpson Hamilton.
Julian Joseph Handler.
Derek Charles Harris.
Francis Alan Sylvester Harris.
Rex Harrison.
Denis Frank Hawkins.
Ernest Stanley Newton Hazel.
Anne Heath.
Rita Henryk-Gutt.
Maurice Druce Heyman.
Robert Franklin Heys.
Evan Peter Hilary-Jones.
James Gordon Hill.
Molly Hill.
William Gerard Holland.
John Albert Hopson.
John Morgan Hughes.
Samuel Hyndman.
Frederick Laidlow Johnstone.
Audrey Jones.
Frank Whitwam Jones.
Richard Joseph Basil Heritage Jones.
John Anthony Kay.
Sylvia Jean Keet.
Robert Michael Bruce Kerr.
Peter John King.

James Alexander Kirkland.
Iris Mary Krass.
Dorothy Kit Chin Kwan.
Zarrin Keki Langdana.
John Frederick Leeton.
Penelope Anne Leighton.
William Gordon Hickman Leslie.
Ewen Hamilton Loxton.
Alan Richards Lyall.
Hugh Douglas MacEwan.
John Alan William McKelvey.
Irene Elizabeth McLaren.
Elizabeth Maude McNab.
Ian Simpson McRobbie.
James Maguire.
Kissundath Mahabir.
Dorothy Mainwaring.
Richard Burton Malcolm.
Eric Mallett.
Pauline Ann Manfield.
Bruce Herbert Markham.
Veronica Mercer.
George Christopher Metcalfe.
John Sidney Bertram Meyer.
John Grant Millar.
Hugh Francis Molloy.
Peter Lawrence Crawford Monier-Williams.
Richard Maurice Armstrong Moore.
Sheila Mary Louise Moore.
Thomas Moore.
James Marshall Munn.
Mira Vinayak Muzumdar.
Brian Ernest Holmes Neal.
Hedley John Leslie Nicholls.
Thomas Mowbray Nott-Bower.
Francis Joseph O'Connell.
Mary Gillian Orrell.
Seaton Chamberlain Paget.
Edward Gray Palmer.
Ponnampalam Paramaswaami.
David Charles Pearson.
Lawson John Thomas Pearson.
Lionel George Pereira.
Frances Katherine Philips.
Alan David Prowse.
Philip Wyndham Quinn.
Freny Anwar Raja.
George Lloyd Sinnett Rankin.
Mohammad Arif Hassan Rayman.
Edward Redfearn.
Kenneth William Reed.
Brian Francis Reeves.
Charles Burridge Rennick.
Hilary Anketell Roach.
Trevor Hunter Roach.
Thomas Leslie Roberts.
Brian Robertson.
George Franklyn Clive Rosser.
Anthony John Rowland.
Shefali Roy.
Norman Derek Royle.
Maurice Frederick Russell.
Betty Victoria Scott.
John Anthony Seddon.
Maurice Semah Shalom.
Claude Alwyn Sharples.
Anthony John Shaw.
James Smith.
Robert Weir Gilmour Stewart.
John Samuel Sugden.
John Forbes Wilson Sutherland.
Edgar Patrick Wylie Tatford.
Geoffrey Arnold Taylor.
Murray George Taylor.
Michael Brierley Teal.
Ann Thomas.
David Keith Morgan Thomas.
Michael Campion Thornton.
Martin Tobias.
Patricia Ann Topham.
Bhanumati Mrigendra Trivedi.
Roger Unwin.
Alice Elizabeth Marie Van Waterschoodt.
James Vernon-Parry.
Alexander Peter Walker.
George Peter Walker.
Edgar Wallace.
Robert Frederick Warnock.
James Roslyn Watson.
Marjory Isabella Katherine Watt.
John Whewell.
Guy Thornton Whitaker.
Joan Winfield Whitaker.
Margaret White.
Agnes Elizabeth Whitter.
James Douglas Wigdahl.
Ian Trevor Denis Williams.
William Anthony Williamson.
Mary Younie.

SYMPOSIUM ON APPLIED EXFOLIATIVE CYTOLOGY

11th–13th JULY, 1957

THIS Symposium, sponsored by the Commission on Cancer Control of the International Union Against Cancer, will be held in the Auditorium of the Federation of Colonial Societies, 34 Rue de Stassart, Brussels, Belgium.

Honorary Chairman: Professor N. Papanicolaou.

All interested in cytology are invited.

REPORTS OF SOCIETIES

THE EAST ANGLIAN OBSTETRIC AND GYNAECOLOGICAL SOCIETY

October 1956

A meeting of this Society was held at the Ipswich and East Suffolk Hospital, on Saturday, 27th October, 1956. The President, Mr. M. W. B. Bulman, was in the Chair.

The main business of the meeting was the reception of two clinical reports by Mr. F. R. Stansfield and a paper by Mr. H. A. Ripman.

A Case of Precocious Puberty

A girl of 5 years of age was referred to the hospital in August, 1955, with a history of intermittent vaginal bleeding and of enlargement of the breasts. The abnormalities were first noted by the mother 8 months previously. At first only slight periodic vaginal bleeding was present, but later the loss lasted from 5 to 7 days and recurred every twenty-eight days. The child's underwear had to be changed at least six times a day during a "period".

The mother stated that the birth of the patient had been normal and that her only illnesses had been a cervical adenitis in 1954 and measles in June, 1955. She had been difficult temperamentally up to the age of 3 years, and then had become docile and affectionate. She had not yet started her school career, and she had not been given any oestrogens.

Inspection revealed a tall, thin, fair-haired girl with marked enlargement of the breasts and pigmentation of the areolae. (Colour photographs of the child were exhibited.) The examination of her cardiovascular system, lungs, and nervous system did not reveal any abnormality, but enlarged cervical lymph nodes were palpated. Scanty pubic hair had developed.

Special Investigations

Vaginal Swab. Polymorphs, epithelial cells, and numerous gram positive bacilli detected. Cultures proved to be sterile.

X-ray of Skull. Pituitary fossa normal. No abnormalities detected.

X-ray of Wrist. Development that of a child of 8 years.

X-ray of Pelvis. Normal for a girl of 10 years.

Differential Diagnosis

The various possibilities were reviewed using the classification suggested by Simpson (1948). Two diagnoses seemed to fit the facts so far ascertained: (1) True precocious puberty of idiopathic origin. This type was first fully reported by Novak (1944) and is probably the commonest form of the syndrome; (2) Iso-sexual pseudo-precocious puberty due to the presence of a granulosa cell tumour of the ovary. Despite the gynaecologist's predilection for such a diagnosis, it is in fact a rare cause.

Examination under anaesthesia. This revealed a uterus about one inch in length that had descended into the pelvis. The left ovary was detected as a tiny flattened mass, whilst the right ovary was replaced by a firm ovoid mass about one and a half inches in greatest diameter. The tumour had neither the consistency nor the shape of a follicular cyst, therefore a tentative diagnosis of granulosa cell tumour of the right ovary was made, and a laparotomy performed. This confirmed the clinical findings. The right ovary was removed.

Pathological report on the tumour. An encapsulated ovoid yellow tumour, measuring 3·5 cm. in greatest diameter replaces the ovarian tissues. Microscopically the tumour reveals a well-differentiated follicular pattern. The cells are filled with an eosinophilic material that gives a positive reaction for fat. This is a benign granulosa cell tumour of the ovary.

Progress. An uneventful recovery followed with regression of the signs of puberty. A brief discussion followed on the effects of the tumour on the other ovary, and on the risks of the development of another tumour, and it was hoped that the child's progress would be watched.

References

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A Case of Post-Abortal Gas Gangrene

A married woman, aged 23 years, was admitted to hospital on 13th April, 1956, on account of ante-partum haemorrhage at the twenty-fifth week of her first pregnancy. She was treated with sedatives in the hope that the abortion was only a threat. The following day there was some diarrhoea, and early on 15th April she had a spontaneous abortion of stillborn uni-ovular male twins. In the evening the ward sister thought the patient was slightly jaundiced. Next day the patient was markedly jaundiced, and was passing only small quantities of chocolate-coloured urine. A clinical diagnosis of a gas gangrene infection of the uterus was made and received confirmation by the subsequent recovery of *Clostridium welchii* in pure culture from the urine and vaginal swab. Blood cultures were sterile.

The patient was isolated, and treated with penicillin and anti-gas serum. Her methaemoglobinaemia was corrected by an intravenous injection of one hundred milligrammes of methylene blue. The blood picture at this time was:

Haemoglobin 44 per cent (6·4 grammes).
Red Cells, 2,440,000 per c.mm.
White Cells, 54,300 per c.mm.
100 per cent Polymorphs.

In former years a white cell count over 20,000/c.mm. was only found in cases that proved fatal. Despite the gravity of her illness she was afebrile. Four days treatment with penicillin cured the infection, but there remained the problem of keeping the patient alive until the liver and kidneys recovered. Our difficulties were increased by the patient's reluctance to swallow any fluid because of the pain produced by a severe oesophagitis, with persistent vomiting. There was persistent myalgia.

The biochemical department carried out daily studies of the patient's blood electrolytes, alkali reserve, blood urea, and haemoglobin level. Simpler measures having failed, a polythene tube was inserted into the inferior vena cava, and through this water, electrolytes, glucose, and blood were given. An attempt was made to keep her in fluid balance, and with an adequate supply of calories in the form of glucose in 50 per cent solution. Recurrent acidosis was partially corrected by infusions of 1/6 molar sodium lactate solution. Nine pints of blood were given during the illness. There was marked oliguria until diuresis set in on 25th April, 1956 after 10 days of renal failure, during which time the blood urea rose to 200 milligrammes per cent and the serum potassium to 34 milligrammes per cent. The serum sodium fell temporarily to 310 milligrammes per cent and the alkali reserve dropped to 32·5 volumes per cent.

The onset of the diuresis brought fresh problems in its train. There was a fleeting rise in the blood urea level, and a precipitous fall in the serum sodium. On 26th April, 1956 it became possible to supply the patient with fluids and food by mouth. Extra salt was given. A normal blood electrolyte pattern was attained by 15th May, 1956.

During this time an *Escherichia coli* urinary infection and a *Staphylococcus aureus* throat infection had to be treated. She was considered, on clinical grounds, to have had a small pulmonary infarction on the left side on 7th May, 1956, but this could not be proved. On 23rd May, 1956 she was fit enough to be transferred to a convalescent home. (Coloured graphs illustrated the biochemical changes.)

Progress

There has been a slow return to normal in the kidney functions. A urea clearance test on 5th October, 1956 gave a figure of 92 per cent of the normal.

Comment

The cause of the abortion and of the infection are unknown. *Cl. welchii* can be recovered from vaginal swabs in 8 per cent of antenatal patients, so it remains a matter of surprise that we only meet with gas gangrene infections of the uterus on rare occasions (Sadusk and Manahan, 1939). Hill (1936) provides a valuable report on the course and treatment of these cases in the days before sulphonamides and antibiotics were available, and the more modern outlook is provided by the report of Mahn and Dantuono (1955).

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Hill, A. M. (1936): *J. Obstet. Gynaec. Brit. Emp.*, **43**, 201.
Mahn, E. H., and Dantuono, L. M. (1955): *Amer. J. Obstet. Gynec.*, **70**, 604.
Sadusk, J. F., and Manahan, C. P. (1939): *J. Amer. med. Ass.*, **113**, 14.

Discussion

The President commented on the absence of fever in this case and asked for the details of the technique for setting up a drip into the inferior vena cava.

Mrs. Townesley reported two cases of post-abortal gas gangrene that she had seen some years ago. Both were fatal. The first case was admitted to a medical ward as suffering from Addison's disease. No doubt they were misled by the patient's bronzed appearance and hypotension. She was treated with the only remedy then available, anti-gas serum, but died in uraemia. It was of interest to record that she coughed up an oesophageal cast. The second patient was moribund on admission to hospital.

Mr. MacKenzie wondered if unsterile vulval pads might be the source of the infection.

Mr. Kimbell had met with 3 abortions from which a swab gave a growth of *Cl. welchii*. These patients were never really ill.

Mr. Harrison reported the case of a woman who had a premature twin delivery and died on the eighth day of the puerperium. She was afebrile and her blood urea was 56 milligrammes per cent. The presence of a gas infection was suspected but not proved.

The President recalled his experience with a patient who aborted a hydatidiform mole and developed a peritonitis. He performed a laparotomy and found free gas in the peritoneum and a twisted ovarian cyst. The twisted left ovary was removed and a cyst enucleated from the right ovary. The patient recovered and has since had two children.

Mr. H. A. Ripman presented

A REVIEW OF THE CAUSES OF STILLBIRTH OVER ONE YEAR IN THE COUNTY BOROUGH OF IPSWICH

The review covered the period 1st July, 1954 to 30th June, 1955, during which time there were 1,837 deliveries and 33 stillbirths: a stillbirth rate of 17·96 per 1,000 total births. It was the object of this retrospective investigation to determine what proportion of the stillbirths were preventable.

Mr. Ripman gave a detailed analysis of the circumstances attending each stillbirth, and grouped them under the following heads:

Gross congenital abnormalities: 7 cases, 21 per cent of the total. These were all of severe degree and incompatible with extra-uterine life.

Strangulation by the cord: 3 cases. One case might have been saved by an induction of labour at full-term as the patient was hypertensive and postmature.

Breech delivery: 2 cases. Study of the case histories did not suggest that these infants could have been salvaged.

Toxaemia: 6 cases.

A detailed study of the histories suggested that in one instance only was there any hope of saving the child, and this would have necessitated the doctor being able to anticipate an accidental haemorrhage in a case of mild toxaemia.

Miscellaneous Causes: 12 cases.

Case 2 The cause of the intra-uterine foetal death is unknown.

Case 5 A case of premature labour at 33 weeks with a prolapsed cord, which was not pulsating.

Case 7 This patient had repeated intra-uterine deaths, the cause being unknown. On this occasion the foetus weighed 1 pound.

Case 12 An intra-uterine death, the cause being unknown. Baby weighed 2¾ pounds.

Case 15 An intra-uterine death, the cause being unknown. The patient avoided antenatal visits by the doctor and midwife.

Case 16 Accidental haemorrhage. Large patent ductus arteriosus. Its diameter was the same as that of the pulmonary arterial trunk.

Case 17 Rubella early in pregnancy. Intra-uterine death.

Case 18 Intra-uterine death. The baby weighed 2 pounds.

Case 25 Diabetes mellitus (unstable). Intra-uterine death. The Caesarean section was delayed because of the instability of her diabetes.

Case 28 Large child. Impacted shoulders caused fatal delay in delivery.

Case 29 Concealed pregnancy. Intra-uterine death.

Case 35 Long labour. Normal delivery. Intra-cranial haemorrhage with bilateral tentorial tears.

The last four babies might possibly have been saved.

Summary

It would be clear that little respect had been paid to the intricacies of recent advances and technical perfections. Mr. Ripman's object had not been to show that in other hands the stillbirth rate could have been smaller. Not every erythroblastosis could pass through Mollison's clinic nor every breech be delivered by a Potter. But he would consider it reasonable to conclude that were common knowledge of authentic value utilized, and a rigid adherence to the accepted standards of antenatal care observed, the stillbirth rate would be brought still nearer to the baseline on the graph.

Discussion

The President wondered if there was really much chance of an improvement in the perinatal mortality. In his opinion a large proportion of these babies were of poor quality and their loss was possibly not to be deplored.

Mr. O'Meara was intrigued by the number of unexplained intra-uterine deaths.

Mr. Stansfield thought that it was misleading to rely on the foetal heart sounds alone. The liquor amnii should be tested from time to time during labour for the presence of meconium. This provided further evidence of the presence or absence of foetal distress. Nowadays resort to Caesarean section in the interests of the baby was justifiable.

Mr. Ripman was not prepared to accept this view except in the case of the elderly primigravida who was postmature.

Mr. MacKenzie wished to have a comparative analysis of the hospital and district perinatal mortality.

GLASGOW OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

December 1956

A meeting of the Glasgow Obstetrical and Gynaecological Society was held in the Rooms of the Royal Faculty of Physicians and Surgeons, on 19th December, 1956.

The President, Professor D. F. Anderson, was in the Chair.

Mr. Robert Newton addressed the Society on

The History of the Manchester Operation

Manchester made no claim to be the original home of the colporrhaphy. In 1888 some gynaecologists in Germany were performing colporrhaphies, and some of them seem to have been composite operations including the amputation of the cervix, anterior and posterior colporrhaphy. There had been considerable discussion as to the parts played by Donald and Fothergill in the origination and development of the operation—because the progress of the operation was one of evolution and improvement, as it is capable of nearly infinite variation. Mr. Newton considered the contribution of these and other Manchester gynaecologists to this surgical treatment of prolapse.

It seems that there is no doubt that Archibald Donald was performing colporrhaphies several years before Fothergill, for on 30th July, 1888, he combined an operation for cystocele and amputation of the cervix with a posterior colporrhaphy. Silver wire was used to bring the flaps together. In his account of the operation (1908), Donald described marking out a triangular flap on the anterior vaginal wall with the base on a level with the vaginal outlet, generally about half an inch from the urethral orifice. But neither Shaw, Dougal, Lacey or Hunter ever saw him perform the operation using this rather curious anterior incision.

Fothergill, said Mr. Newton, wrote clearly and well and it was easy to trace the development of the operation in his hand, both by his lucid writings and his able line-drawings and sketches. In 1907 Fothergill read a paper to the Royal Society of Medicine in which he described the main supports of the uterus. In his opinion the uterus was solely supported by the condensation of fibrous tissue around the uterine vessels. He suggested that the levators ani and coccygi were atrophic and mainly useless. In the discussion, however, Herbert Spencer did point out that the ligamentum colli was a dense structure lying at a lower level than the uterine artery.

In the same *Journal of Obstetrics and Gynaecology* in which Donald in 1908 first described his combined

colporrhaphy, Fothergill described his first modification of the anterior colporrhaphy. By using a triangular incision he claimed to unite the parametric and paravaginal tissues to one another and to the anterior aspect of the cervix, thus effectively shortening the supports of the cervix. In 1914 he described the operation more or less in its fully developed form. Fothergill marked out his anterior incision by means of four forceps, one below the urethra, one on each side of the cervix and one behind the cervix. A kite-shaped incision was performed, the top of the kite encircling the cervix: the anterior flap was dissected off from just below the urethra to the cervix. He was careful to produce sufficient flaps around the cervix both at the sides and at the back to cover it completely. He began stitching behind the cervix and worked around and forwards. The stitch came to be known in Manchester as the Key Suture of Fothergill. Then he brought the lateral flaps of the vaginal skin and the deeper fascia together with one stitch in front of the cervix. He then stitched up the anterior incision with single sutures. It is said that he often remarked that the more roughly the operation was performed, the better the result.

Fothergill wrote of Donald: "He had also brilliantly combined the operation of posterior colporrhaphy and perineorrhaphy in a single operation done from above downwards. For the past thirty years Donald has cured an enormous number of cases of prolapse by amputation of the cervix, extensive anterior colporrhaphy and his own colpo-perineorrhaphy. My own contributions to the surgery of prolapse were made at a much later date."

Sir William Fletcher Shaw has insisted on the use of the deep tissues separately from the mucosa. The mucosa was united by means of a continuous blanket suture. He relied on the deep sutures to produce a firm support for the prolapsed pelvic structures. He dissected the bladder upwards from off the uterus; the connective tissue thus exposed on either side of the isthmus of the uterus was picked up by two deep sutures which were left and tied later. After the cervix was amputated and covered with vaginal epithelium, the deep sutures were tied and the anterior incision closed by a continuous suture. As the incision was being closed more deep sutures were inserted as necessary. The posterior incision was wide-angled and began just below the cervical stump. The peritoneum of the Pouch of Douglas was pushed backwards and the first sutures inserted quite deeply to cure or prevent the occurrence of enterocoele.

Dougal would insert "Kelly-like" sutures if there was any complaint of stress incontinence. He made many layers in the repair of the perineum which he often advanced until it was just short of the urethra. When dealing with younger women, Dr. Hunter left the cervix undamaged by recessing it, so to speak, in the vault of the vagina by taking a ring of epithelium away around the cervix. Dr. Brentnall frequently reduced the bulk of the cervix by removal of an anterior wedge of the cervix—a method first used by Fothergill.

Mr. Newton said that the foregoing account illustrated the capacity for modification inherent in the Manchester operation and herein lay the secret of its great success. He speculated as to how colporrhaphy cured prolapse. He suggested that the formation of a normally-shaped vagina was important, It acted as a "core in a casting", and round it, forming the casting itself, is the crimped and crumpled connective tissue which held the vagina and uterus in a normal position. The factor which temporarily retained the vagina in position was the plastic repair and narrowing of the vagina.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

January 1957

The Annual General Meeting of the North of England Obstetrical and Gynaecological Society was held in Manchester on 18th January, 1957. The following were elected Officers for the year.

President—Mr. F. Stabler.

Vice-Presidents—Dr. E. A. Gerrard (Manchester), Mr. P. Malpas (Liverpool), Mr. H. Agar (Leeds), Mr. G. R. MacDonald (Sheffield), and Dr. W. Hunter (Newcastle).

Hon. Treasurer—Mr. C. H. Walsh.

Hon. General Secretary—Mr. F. J. Burke.

Hon. Reporting Secretary—Miss U. M. Lister.

Dr. J. Firth read a case record of

MASSIVE POST-PARTUM HAEMORRHAGE ASSOCIATED WITH AFIBRINOGENAEMIA

(This article appears on page 385 of this issue)

Discussion

Mr. C. H. Walsh expressed interest in these cases and asked why a dettol douche was used. He thought it difficult to prove an amniotic fluid embolus.

Dr. J. S. Scott asked what method was used for the fibrinogen estimations as results vary so widely with the method used. Some bloods to which active thrombin is added will produce no clot until incubated with calcium. Fibrinogen is not absent in these cases, but present in a form that will not react with thrombin.

It was implied that uterine retraction was not good, and that this was a factor in the post-partum haemorrhage, especially as the bleeding ceased with the hot douche.

Mr. J. F. Redman brought up the problem of the missing blood. Eleven pints of blood were transfused, and at the end the haemoglobin was 54 per cent. This suggested a loss of 15 pints.

Mr. J. B. Cochrane asked why fibrinogen was not given instead of plasma, and if ergometrine was used prophylactically when it was known that there was difficulty in clotting.

In his reply Dr. J. Firth said that a hot douche was given on general principles. The fibrinogen estimations were done by the Pathology Department. Fibrinogen was difficult to obtain, but plasma was readily available, Ergometrine was given as soon as the bleeding started. but it might well have been administered with the anterior shoulder.

Mr. D. W. Currie showed a film on

RADICAL HYSTERECTOMY FOR CARCINOMA OF THE CERVIX

Before showing the film Mr. Currie presented the results of his operation.

Total Cases 214; Deaths 51.

5-year survival rate	..	81 per cent (22 died out of 118)
10-year survival rate	..	78 per cent (10 died out of 46)
5-year survival rate of those with glands	..	55 per cent (12 died out of 27)

Stages

Stage 1	97 cases
Stage 2a	83 cases
Stage 2b	25 cases
Stage 3	9 cases

5-year survival rate of Stages 1 and 2a—88·4 per cent (91 out of 103).

10-year survival rate of Stages 1 and 2a—89·6 per cent (34 out of 38).

Involvement of Glands

Stage 1	15·4 per cent
Stage 2a	32·6 per cent
Stage 2b	60·0 per cent
Stage 3	88·0 per cent

Discussion

Mr. C. H. Walsh expressed admiration for the artistry of the surgeon. He asked if radium was usually employed, and commented on the method of mobilizing the ureters.

Dr. R. Newton spoke of the very high quality of the photographic technique.

Mr. C. J. K. Hamilton who had seen a similar operation thought it was done just as well when not being photographed.

Mr. T. B. FitzGerald asked for information on the approach to the obturator fossa.

Dr. J. W. Hunter commented on the knowledge of anatomy required. There was a tendency to approach the ureter from the lateral aspect. He thought this might deprive it of too much of its blood supply, and asked if Mr. Currie's method ever gave trouble in this respect.

Mr. F. Da Cunha asked if it was an advantage to fashion a vaginal cuff from below.

Professor W. I. C. Morris mentioned the many techniques for this operation. Across the Atlantic there is a more radical approach and a mass of paracervical tissue is removed. Meigs reported fistulae in 8 per cent of cases, and his patients left hospital with a catheter *in situ* which they needed for 3 months. These radical measures may cause lasting damage.

Mr. C. J. Dewhurst asked about the anaesthetic, and what should be done if there was injury to the iliac vessels.

Mr. Currie replied.

Pre-operative radium was used in 180 cases, and in more than half these cases one-third of the lethal dose had destroyed the primary growth. In no case were involved glands affected by the radium. After a full dose of radium dissection was more difficult, and he proposed to dispense with it, and give deep X-ray therapy to those cases with positive glands.

In the 5 cases where fistulae had developed, 2 were not really at fault, and 1 closed on its own.

Cloquet's gland had been the only positive gland in 3 cases. Mr. Currie used to clean the fat off the pelvic floor and look for pararectal and sacral glands, but ran into so much trouble that he has abandoned it. He removed the obturator glands by a finger in the fossa.

Mr. Currie never cleaned the ureter, and he treated the bladder as a "cussed" organ that required a catheter. The cuff operation was abandoned many years ago. Injury to the iliac vessels was rare, but they might have to be tied.

The anaesthetics employed included hibernation. Glucose in normal saline was started, blood replaced, and the transfusion stopped that night.

BOOK REVIEWS

"The Queen Charlotte's Textbook of Obstetrics." 9th Edition. Pp. xi+547, with 4 coloured plates and 246 text figures. J. & A. Churchill, Ltd., London. 1956. Price 45*s*.

THE new edition of this popular book maintains the practical quality of previous editions. The photographs of histological sections are particularly good in the chapter on eclampsia, and throughout the illustrations are adequate.

In any textbook certain topics must be stressed at the expense of others, and this book would gain by addition to the section on maternal physiology.

The task of correlating the contributions of many members of the clinical staff is a difficult one, and there is a certain lack of such correlation. This is apparent when references are made to cardiac output in pregnancy, and again to the most opportune moment for performing Caesarean section in cases of abnormal uterine action.

The section on pyelitis in pregnancy could be better correlated with that of pyelitis in the puerperium, and the danger of crystalluria during treatment with sulphonamides is mentioned in neither, although it is stressed in the chapter on puerperal fever.

Intramuscular rather than intravenous iron is now commonly used for iron-deficiency anaemia, but this is omitted.

Reference to the contra-indications of external version might well be added in a subsequent edition, and also to the risk of infective endocarditis in cardiac cases during the puerperium.

One omission could well be that of the illustration depicting the questionable use of Willett's forceps during lower segment Caesarean section.

The chapter on puerperal fever is outstanding. The section on trial labour is perhaps one of the clearest in all the numerous textbooks on obstetrics. The section on the baby is comprehensive, and there is an excellent chapter on the Rhesus factor.

This remains a most readable book, well laid out and written with utmost clarity. It will rightly enjoy continued support.

"Human Ovulation and Fertility." By EDMOND J. FARRIS, Ph.D., Director, Wistar Institute of Anatomy and Biology, Philadelphia. Pp. xiii+159, with 56 tables and 35 figures. Pitman Medical Publishing Co., London. 1956. Price 50*s*.

THIS book, which details the results of the author's researches into the problems of ovulation in the human and discusses their clinical application, centres round the Farris test for ovulation. The test is based on the production of hyperaemia in the ovaries of immature rats by the injection of urine from a woman at the time of ovulation. The value of the test is supported by corroborative evidence obtained at laparotomy and by the high degree of correlation with histological dating from endometrial and ovarian tissues.

The author reaches several interesting conclusions. He adduces evidence to show that the postovulatory phase of the menstrual cycle is not relatively fixed at about 14 days but ranges more widely from at least 9 to 19 days; that the time of ovulation cannot be determined accurately by basal body temperature charting; and that ovulation occurs about 2 days prior to mid-cycle, whatever the length of the cycle, rather than about 14 days before the next period. Supported by data from over 100 pregnancies with a known date of conception after natural or artificial insemination, he propounds schemes for the determining of the optimum time for conception and for the calculation of the "safe period". The author also describes a pregnancy test depending on the colour-matching of the cervix with standard colour strips.

All those concerned with the physiology of human reproduction and the management of infertility will read this book with sustained interest if not with unfailing conviction.

"Human Generation: Conclusions of Burdach, Döllinger and Von Baer." By A. W. MEYER, Professor Emeritus of Anatomy, Stanford University, U.S.A. Pp. x+143. Stanford and Oxford University Press. 1956. Price 28*s*.

THIS is an annotated translation of a series of works on biology which appeared in the early 19th century: "Concerning the First Changes in the Formation of a Foetus", and "Anatomical Annotations on the Human Foetus" (Burdach); "Attempt at a History of Human Reproduction" (Döllinger); and "Commentary on the Writing on the Eggs of Mammals and Man" (von Baer). There is an account of the life and work of each of these biologists, with Professor Meyer's main interest lying apparently in von Baer. This work will appeal to those interested in the history of zoology and human embryology.

REVIEW OF CURRENT LITERATURE

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PHYSIOLOGY

134. **A Study of the Effect of Relaxin on Contractility of the Non-Pregnant Uterus by Internal Tocometry.**

By N. Posse and J. V. Kelly. *Surg. Gynec. Obstet.*, **103**, 687–694. Dec. 1956. 4 figs. 25 refs.

Fifty normal women were investigated at various stages of the menstrual cycle, employing the intra-uterine electro-hysterographic method of Karlson with micro-carbon receptors in the fundus, isthmus and cervix.

The relaxin used in this study was supplied as releasin. It was furnished in 2 ml. vials, each ml. containing activity equivalent to 20 mg. of relaxin reference standard —or 3,000 guinea-pig units per ml. The intravenous route of administration was employed. The dosage varied from 0·5 to 14·0 ml., the average initial dose was 2 ml. and the average total amount of relaxin given to each patient was 10 ml.

Twenty-eight cases were in the proliferative phase of the cycle at the time of investigation. Tocometric recordings revealed the same general pattern of uterine contractility in all. It was characterized by moderate tonus in the fundus and isthmus with superimposed contractions of small amplitude and high frequency. Cervical motility was generally confined to small irregular contractions. This pattern was observed in each case for approximately 1 hour and then the relaxin was given. In 24 of the 28 patients there was an immediate reduction in uterine motility persisting for 40–60 minutes. The 4 patients on whom relaxin had no effect were all studied at approximately the time of ovulation.

In the 14 women in the secretory phase of the cycle at the time of investigation, tocometric tracings exhibited in all the same general pattern of uterine contractility. It was characterized by synchronous contractions in the fundus and isthmus of large amplitude and relatively low frequency. Tonus was usually slight or absent and the cervix was generally inactive. After an hour of observation relaxin was given, and in only 8 cases was there a reduction of motility.

Recordings were made during the first to third days of painful menstrual periods in 8 patients. In all cases the general contractility pattern was similar. This was characterized by fundal contractions of large amplitude and fair duration which were usually coincident with the pains felt by the patient. Surprisingly there was nearly complete absence of isthmal activity and of fundal or isthmal tone. The cervix exhibited a high degree of tonus in most cases with small superimposed contractions. In 7 of the 8 patients, following the administration of

relaxin, there was a marked reduction in the amplitude, frequency and duration of the contractions accompanied by definite relief of pain.

In all the cases in which relaxin was administered it was noted that the uterus rapidly developed tolerance to the drug, so that repeated administrations even in increasing amounts had less effect or no effect whatever.

The authors discuss the hormonal control of uterine motility and suggest possible explanations for the decreased effectiveness of relaxin during the secretory phase of the cycle. *John P. Erskine*

PREGNANCY

135. **Investigations on the Accuracy of the Hyperaemia Test of the Rat Ovary for Pregnancy Diagnosis.** (Untersuchungen über die Eignung der Hyperämietestes am Rattenovar für die biologische Diagnose der Schwangerschaft.)

By H. Borth, B. Lunenfeld, G. Riotton and H. de Watteville. *Arch. Gynäk.*, **188**, 112–122. 1956. 2 tables. 25 refs.

Tests were carried out on 550 female infantile rats, varying in weight from 35–45 g. They were injected with 2 ml. of 0·9 per cent saline (control animals), 2 ml. of urine or 1 : 1 diluted serum, or 0·08–40 i.u. of a standard chorion-gonadotrophin, prepared from pregnancy urine and dissolved in 2 ml. normal saline. The injections were given intra-peritoneally, half the amount into the right and the other half into the left inguinal regions. The animals were killed 6 hours after injection by gassing and their ovaries inspected in daylight.

The degree of sensitivity to gonadotrophin varied widely with each individual rat. The liminal concentration tested in pregnancy tests varied within an even greater margin, i.e., 660–8,000 i.u./l. urine. The mean excretion of gonadotrophins in a normal pregnancy averages 600 i.u./24 hours, 4–5 weeks after the last menstrual period, but exceeds 6,000 i.u./24 hours between the 6th and the 7th week. Peak excretion (about 20,000–400,000 i.u.) occurs between the 7th and 12th week, and from about the 15th week the average daily excretion remains stable at about 8,000 i.u./24 hours.

It is, therefore, clear that the sensitivity of the hyperaemia test is sufficient to be utilized in pregnancy tests from the 7th week onwards.

On 139 cases simultaneous rat and Friedman tests were carried out; there was good correlation in 130 cases, i.e., 94 per cent. One of the 9 cases, where no correlation was obtained, was a definite false negative rat test, in 1 no details were available, and in 7 the pregnancies were abnormal.

The authors recommend the use of the hyperaemia test as a rapid and simple pregnancy test. They consider it advisable, however, to test the variations of sensitivity in the rats at regular intervals and to use 3–5 animals for each test. *E. Wachtel*

136. **Exact Evaluation of Anatomical Relationships. (A New Orthodiagraphical Method Designed Particularly for Obstetrical Radiology.)**

By C.-E. Johanson. *Ann. chir. gynaec. fenn.*, **45**, 290–295. 1956. 5 figs.

Complicated formulae are required to convert pelvic measurements taken from the X-ray plate into the actual measurements of the patient, due to the divergent beam of X-rays. The author has devised a simple apparatus whereby a band of X-rays only 1·1 mm. wide is made to traverse the patient's pelvis. There being no divergence, the actual pelvic measurements may be read directly from the film. The author recommends high voltages 150–180 Kv but owing to increased screening the average dose is only 0·2 *r*. Considerable accuracy of measurements is claimed. *D. M. Sheppard*

137. **Diagnostic X-ray Dosages in Obstetrics.**

By C.-E. Johanson and M. Viikeri. *Ann. chir. gynaec. fenn.*, **45**, 296–302. 1956. 13 refs.

In animal experiments foetal malformations are only produced by irradiation during the period that corresponds to the second to sixth week of human pregnancy, often a time when the pregnancy may not even be recognized. A minimum of 25 *r* may have harmful effects but a dosage of 3 *r* per ovary will not produce mutations. The authors devised an ionization chamber on a tube which could be inserted high up in the rectum at the level of the ovaries. The mean dosage received in this region after four exposures during pelvimetry was 0·535 *r*. The authors consider that with modern technique and screening the risk to the foetus and ovaries is negligible. They recommend, however, the avoidance of X-ray examination in early pregnancy or where pregnancy is suspected. *D. M. Sheppard*

138. **A Method of Radiocephalometry.** (Une méthode de radiocéphalométrie.)

By P. Rosa. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 676–701. 1956. 16 figs.

The author describes a new method of radiocephalometry, intended to determine the bi-parietal diameter of the foetal skull, in breech as well as in cephalic presentations. The method depends on the correct orientation of the photographic level, perpendicular to the plane of symmetry of the foetal head. Then two radiographs are taken, the patient being turned 180° between exposures. The real value of the measured diameter is found by calculating the arithmetic mean of two measurements made on the radiographs, using a prepared scale. The method is independent of the distance of the X-ray source and renders negligible the error resulting from the obliquity of the X-rays. *Author's Abstract*

139. **Roentgenologic Localization of the Placenta in Late Pregnancy.**

By C.-E. Johanson and M. Viikeri. *Ann. chir. gynaec. fenn.*, **45**, 279–289. 1956. 12 figs. 16 refs.

The authors report on the results of soft tissue radiology in localizing the placental site while using an aluminium filter and a compression device. Of 200 cases

investigated with X-rays prior to the use of the filter in only 82·5 per cent of the cases was the placenta visualized. Of 400 cases examined with the use of the filter, in 96·75 per cent, the placenta was visualized. The causes of failure to visualize the placenta are discussed.

D. M. Sheppard

140. **Aortography: the Safest Means of Placental Localization? A Preliminary Report.**

By P. D. DE VILLIERS and D. BRINK. *S. Afr. med. J.*, **31**, 37–40. Jan. 12, 1957. 4 figs. 12 refs.

Mistakes are apt to occur when localization of the placenta by soft tissue radiography is used in the average department. The authors have examined 25 cases of ante-partum haemorrhage by transfemoral aortography. They claim that it is the safest method—if radiation hazard is given due importance. It is the simplest method with the help of Seldinger's apparatus, and it is the most accurate method in the hands of the inexpert interpreter.

The technique is described and it is said to be surprisingly easy. Nine inches of catheter is introduced and 20–25 ml. of 50 per cent Diaginal is injected as rapidly as possible. Sensitivity tests were done and there were no untoward effects. A single picture, taken 1½–2 seconds after completion of the injection, indicates the placental site clearly in most cases. The authors prefer a single lateral view to the antero-posterior projection.

In no case did labour commence within the first day following the investigation, as had been stated to occur when 70 per cent Diodrast or 80 per cent sodium iodide was used. The biggest advantage of aortography may be that the examination requires only a single exposure. The possible complications of translumbar aortography are mentioned.

L. J. Abramowitz

141. **The Protein Content of the Liquor Amnii at the End of Pregnancy.** (Il contenuto proteico del liquido amniotica a termine di gravidanza.)

By G. B. CANDIANI. *Ann. Ostet. Ginec.*, **78**, 475–480. 1956. 2 tables. 3 figs.

The protein content of the liquor amnii at term has been determined. Liquor was obtained by aspiration with a syringe at full dilatation of the cervix. This was compared with maternal and foetal serum. Observations were made in 25 cases.

It was found that the total protein content of the liquor amnii was always significantly lower than that of maternal and foetal serum. The percentage of albumin and beta-globulin was consistently higher in the liquor amnii than in maternal and foetal serum, with an almost total lack of gamma-globulin in the liquor. The albumin/globulin ratio is consistently higher in the liquor amnii than in the maternal or foetal serum. It is concluded that the liquor is primarily a transudate and has a purely mechanical function.

Josephine Barnes

142. **Clinical Significance of Weight Trends During Pregnancy.**

By A. M. THOMSON and W. Z. BILLEWICZ. *Brit. med. J.*, **1**, 243–247. Feb. 2, 1957. 3 tables. 1 fig. 15 refs.

Information was obtained by studying 4,214 primigravid women resident in the City of Aberdeen and delivered in the Aberdeen Maternity Hospital as booked cases during the six years 1949–54. (No case of multiple pregnancy was included in this number.) No attempt was made to restrict the amount of weight gained by these patients.

Patients were weighed at the first antenatal visit and again four to six weeks later. Most of them were subsequently weighed at monthly intervals until 28–30 weeks of pregnancy and more often during the final weeks. Accurate lever balances were used and patients wore underclothes only. For each patient weights in the 13th, 20th, 30th and 36th weeks were determined and the average weekly rates of gain in the three intervening periods calculated. These average weekly rates of gain were the data used for most purposes.

For purposes of analysis the records were divided into three clinical groups: (*a*) Cases of pre-eclampsia with albuminuria (6·5 per cent); (*b*) Cases with other hypertensive complications (25·4 per cent); (*c*) Cases without hypertensive complications (68·1 per cent).

It was found that in normal pregnancy the average total weight gain was 27·6 pounds (12·5 kg.) and that the average rate of gain in the period 30–36 weeks was 0·87 pounds (395 g.) a week.

Patients who developed pre-eclampsia were found to have a higher average rate of gain in weight than those whose pregnancies were normal. As the rate of gain rose the incidence of pre-eclampsia increased, but in individual cases study of the rate of gain over a period of time such as 20–30 weeks was of little prognostic value.

Where weight gains were consistently low the incidence of prematurity was high. As the rate of gain increased, the incidence of prematurity was found to fall but it rose again when rates of gain were high. In the latter group only was pre-eclampsia an important cause of prematurity.

As regards prematurity the authors conclude that women who fail to gain an adequate amount of weight, present at least as important a problem as those who gain excessively. They consider that vigorous restriction of weight gain is not justifiable and may be harmful. Having in mind the hazard of pre-eclampsia on the one hand and prematurity on the other hand, they suggest a weight gain of ¾ to 1¼ pounds (340–567 g.) a week, at least throughout the second half of pregnancy, as a realistic average to aim at.

R. W. Grayburn

143. **Does the Eclamptic Syndrome Lead to Persistent Organic Damage?** (Hinterlässt der eklamptische Symptomenkomplex Organschäden?)

By G. DÖDERLEIN and H. SCHMIDT. *Zbl. Gynäk.*, **79**, 1–19. Jan. 5, 1957. 14 tables. 29 refs.

The authors put the question whether vascular, renal or hepatic damage observed after pregnancy is the direct result of pregnancy toxaemia or is due to pre-existing disease.

Of 100 women who had suffered from eclampsia or pre-eclamptic toxaemia within the previous 10 years, 32 agreed to be admitted to the gynaecological clinic of the University of Jena for investigation.

In 7 out of 17 cases of previous eclampsia and in 6 out of 15 cases of pre-eclamptic toxaemia a history suggestive of previous renal damage was obtained (1 case of mobile kidney, 1 case of renal contusion, 3 cases of pyelitis of pregnancy, 1 case of hypertension and 7 cases of scarlet fever). As regards previous liver damage, 2 of the 17 cases of eclampsia gave a history of "subicterus" and of hepatitis respectively. Of the 15 cases of pre-eclamptic toxaemia one had suffered from gastritis with achlorhydria and as many as 6 patients gave a history of hepatitis.

The patients were examined clinically. In all cases the results are reported of blood pressure estimation, urinalysis, renal and hepatic function tests.

The authors conclude that the toxaemias of late pregnancy do not *per se* leave permanent damage to the kidneys, liver and vascular system. In cases of toxaemia superimposed on pre-existing disease the prognosis is less favourable.

They advise that during antenatal supervision a sharp look-out should be kept for patients with pre-existing disease. These should be treated under the joint care of the obstetrician and the general physician.

Bruce Eton

144. **Variation of Thrombocyte Count in Labour in Healthy and Toxaemic Women.** (Über die Schwankungen der Thrombocytenzahl während der Geburt bei gesunden und bei toxämischen Frauen.)

By P. VARA and K. KOTSALO. *Ann. chir. gynaec. fenn.*, **45**, 251–263. 1956. 5 figs. 22 refs.

The thrombocyte count was estimated in 70 gravid women, at the end of pregnancy, during labour and up to the fourth day of the puerperium. Thirty-eight women were healthy and the remaining 32 were toxaemic. In the healthy patients there was a significant fall in thrombocytes in the last days of pregnancy and during labour rising again to normal in the first four days of the puerperium. In the severe toxaemia there was no such fall but rather a rise over the same period. Similar changes, but not to significant degree were seen in the milder toxaemias. The author suggests that the excess thrombocytes in toxaemia may produce intravascular clumping of erythrocytes with production of hypo- or afibrinogenaemia.

D. M. Sheppard

145. **Photoplethysmographic Recordings Before, During and After Delivery in Cases of Pregnancy Toxaemia.** (Ricerche fotopletismografiche eseguite prima, durante e dopo il parto in casi di nefropatia ipertensiva.)

By G. V. VALENTI. *Ann. Ostet. Ginec.*, **78**, 461–70. 1956. 1 table 3 figs. 30 refs.

The photoplethysmograph has been used to measure the pulse pressure in the right hand in normal pregnancy, labour and the puerperium and in cases of toxaemia of pregnancy.

In normal pregnancy, pulse pressure is relatively low, but there is an increase during labour which persists into the puerperium. In toxaemia the pressure is raised at the end of pregnancy. During labour in normal and toxaemic women, a marked rise occurs with each uterine contraction. After delivery, the pressure is higher in toxaemic women for the first two days, but falls to that of normal women by the third day.

It is concluded that in cases of toxaemia there is a general increase in the peripheral circulatory resistance and that this is associated with hypertension.

Josephine Barnes

146. **Bleeding from the Marginal Sinus in a Case of Placenta Circumvallata.** (Randsinusblutung bei Placenta circumvallata.)

By R. MEY. *Zbl. Gynäk.*, **79**, 73–79. Jan. 12, 1957. 1 fig. 24 refs.

The author describes the case of a pregnant woman who bled during the second month and again at 27 weeks. She delivered herself at 28 weeks and collapsed owing to bleeding during and after the third stage of labour. She recovered with blood transfusion and oxytocic drugs. The placenta was of the circumvallate type. The peripheral zone outside the ring was 3–4 cm. wide and covered with thick old and fresh blood clots.

The author believes that placenta circumvallata predisposes to bleeding in pregnancy from the marginal sinus, because the peripheral part lacks the normal protection of the membranes. The separation may be due to traction by the membranous attachment resulting from changes in uterine tone.

He regards bleeding from the marginal sinus as an important entity and discusses the diagnosis which depends largely on exclusion of placenta praevia and accidental haemorrhage due to toxaemia. Bleeding from the marginal sinus mostly starts in the second trimester of pregnancy and tends to be continuous, whereas in cases of placenta praevia it tends to be intermittent.

[These views are based on the recognition of the existence of the marginal sinus as described by Spanner. Recent studies by Hamilton and Boyd (*Proc. R. Soc. Med.*, 1951, **44**, 489) of placentae *in situ* showed no evidence for the existence of the marginal sinus.]

Bruce Eton

147. **Histological Changes in the Uterine Cervix in Abortion and the First Stage of Pregnancy.**

By C. v. NUMERS and L. LEHTO. *Ann. chir. gynaec. fenn.*, **45**, 228–236. 1956. 10 refs.

Biopsies of the squamo-columnar junction of the cervices from 27 cases of abortion and 25 cases of normal pregnancy were taken and studied. Basal cell hyperactivity was seen in 12 out of 27 abortion cases and in only 3 out of 12 normal cases. In 5 out of 10 cases followed up 3–5 months afterwards this change had persisted. Epidermization of columnar epithelium and gland hypertrophy was seen but was rare. No correlation between hyperactivity and duration of pregnancy was observed. The relationship of basal cell hyperactivity to carcinoma of the cervix was discussed. Persistent hyperactivity may possibly have a bearing on carcinoma.

D. M. Sheppard

148. **Pathogenesis and Therapy of Acute Renal Failure with Anuria Following Abortion in a Case in Which the Toxic Effects of Soap Paste Could be Excluded.** (Über Pathogenese und Therapie der akuten Niereninsuffizienz mit Anurie nach Abort unter Ausschluss der Siefenintoxikation.)

By W. Soergel. *Zbl. Gynäk.*, **79**, 107–111. Jan. 19, 1957. 19 refs.

Following diagnosis of intra-uterine death of the foetus at 27 weeks quinine was administered; this resulted in abortion, intravascular haemolysis, and anuria lasting 26 hours. As criminal interference was excluded the haemolysis was attributed to allergic reaction to quinine which the patient had received in previous years. The haemolysis contributed to a condition of severe shock with generalized anoxaemia in an already anaemic patient.

The author believes that the anuria was due to "lower nephron nephrosis". The patient responded to treatment with blood transfusion, intravenous hydrocortisone, terramycin, glucose and calcium. *Bruce Eton*

149. **The Pathology of Foetal Membranes in Late Abortions and Premature Labours.** (Pathologie des membranes ovulaires dans les avortements tardifs et les accouchements prématures.)

By C. Stamm and G. Riotton. *Gynaecologia, Basel*, **142**, 331–336. Nov. 1956. 6 figs. 7 refs.

At the Geneva Clinic the authors have done urinary estimations of placental hormones in cases of spontaneous abortion and premature labour. Their findings resembled those of other workers. They quote Seguy and Jayle who found that only 30 per cent were associated with deficient hormones, and Watteville who examined 50 cases going into labour between the 16th and 37th week. Twenty per cent had severe lutein deficiency and in 30 per cent the pregnanediol level was low normal, but 50 per cent showed no progesterone deficiency.

The authors compared endocrine levels with histological appearances of the placenta and proved that lutein deficiency was generally associated with multiple placental infarcts, sclerosis and hyaline changes in the villi (8 out of 10 cases). On the other hand these lesions were rare when the pregnanediol level was normal (3 out of 15 cases).

When abortions occurred without placental changes or endocrine deficiencies, they noted that the pregnant woman often had some general illness, pregnancy complication, or anatomical or functional abnormality of the myo- or endometrium.

Because Stamm had shown in experimental work on hydramnios that chemical, trophic or inflammatory changes in the maternal and foetal membranes could cause abortions, the authors decided to examine in histological detail the membranes from cases of abortion and premature labour, and in this article give a preliminary report.

(1) In cases where a normal pregnancy was interrupted by hysterotomy or Caesarean section before term the membranes were healthy. The amnion was covered by a layer of cubical epithelium without lipoid inclusions. The chorion and decidua consisted of many layers of polygonal cells, with a vesicular nucleus showing no degeneration. Necrotic areas were rare and leucocytes seldom seen.

(2) After spontaneous labour at term the amnion was partially necrotic, the epithelial cells containing lipoid globules. The chorion and decidua were strewn with necrotic areas and the cells showed varying degrees of lipoid degeneration. Leucocytic areas were exceptional.

(3) In late abortions and premature labours with late or early rupture of membranes, the most common change in the membranes was inflammatory, i.e., leucocytic infiltration with necrosis, oedema and hyperaemia. In addition there were degenerative changes similar to those found at term.

The authors describe 2 typical cases:

(*a*) At 30 weeks pregnancy, a woman developed acute appendicitis and was operated on; the appendix had not perforated. Four days later she went into labour. The membranes showed many necrotic areas surrounded by a zone of leucocytes and hyperaemia. They postulate that the endometrium had been infected from the bloodstream.

(*b*) An apparently normal woman had labour pains at the 30th week. At the 32nd week she had a spontaneous delivery, the membranes rupturing late. Macro- and microscopical examination of the placenta was normal but the membranes showed leucocytic infiltration. The baby died on the 3rd day, and autopsy revealed a purulent otitis media, meningitis and broncho-pneumonia.

They suggest that the foetus was infected by virulent organisms in the endometrium and possibly also during labour from infected cervical and vaginal secretions.

In some cases where the membranes appeared normal, subchorionic and decidual haemorrhages were seen, due to partial separation of a normally situated placenta or rupture of a marginal sinus.

The authors conclude that late abortions and premature labours are frequently associated with inflammation of the membranes due to a bloodstream or ascending infection. The organisms can also infect the foetus. Therefore they suggest that in cases of threatened premature labour, especially if there is a leucocytosis and high sedimentation rate, antibiotics should be given. They should also be given in all cases of inevitable premature labour in the interest of the baby.

Jean Hallum

150. **Heart Disease in Pregnancy.**

By E. M. Sandler. *S. Afr. med. J.*, **31**, 70–77. Jan. 26, 1957. 23 tables. 16 refs.

The author has studied 187 cases of heart disease in pregnancy. These patients were under the care of the Teaching Maternity Units of the University of Cape Town in the 3 years 1952–1954. The incidence of 0·8 per cent is compared with that of London and Dublin hospitals. Thirty-seven cases (19·8 per cent) were "non-booked". The types of heart disease are enumerated, and probably over 90 per cent were of rheumatic origin. Management during pregnancy is discussed. Grades 1 and 2 should be seen frequently and complications should

be prevented. The cardiac burden is maximal from the 28th to the 32nd week. Patients in grades 3 and 4 should be admitted to hospital for the duration of the pregnancy. Should there be no improvement with medical treatment in grade 4 cases, valvotomy or termination must be considered. Coarctation of the aorta calls for Caesarean section because of the risk of rupture.

Many authoritative views are presented on termination of pregnancy. Most people feel that there is a place for termination, and that it should be carried out before the 20th week. The advent of the operation of valvotomy has produced a modification of views. The results of the non-interventionists do not appear to be any worse than those in which therapeutic abortion is practised. In this series pregnancy was terminated in 4 cases (2·1 per cent), at 15, 12, 20 and 9 weeks. Abdominal hysterotomy and sterilization was performed in each case. In 3 patients the main indication was hypertension.

The place of valvotomy is not yet clear. Dramatic results may be produced. Some authorities feel that there is an added risk in pregnancy. There is still uncertainty about the immediate response to valvotomy. Wood's criteria are quoted. The operation was performed twice in the Cape Town series, and 1 patient aborted.

The incidence of forceps delivery was 5·6 per cent as against 4·9 per cent for all cases. The Caesarean section rate was 3·9 per cent as against 6·0 per cent for all cases. These figures are compared with those of Queen Charlotte's Hospital. There were 4 maternal deaths in the cardiac cases, an incidence of 2·1 per cent, which was seven times higher than the death rate for all cases. These cardiac deaths were responsible for 5·8 per cent of all the maternal deaths. Heart disease was fourth in importance as a cause of maternal death. Comparison is made with British hospital records. The deaths are discussed, and the author suggests that 3 may have been prevented by stricter antenatal supervision.

The natural history of mitral stenosis and the functional grades are discussed. There was a "shift to the left" at the time of delivery, showing an improvement in the functional grade during pregnancy. There was little difference between the under-30 and over-30 age groups. The stillbirth rate was the same as for all other cases. The views of various authors on the effect of pregnancy on rheumatic heart disease are discussed.

If pregnancy is terminated it must be done before the 20th week. The author has extreme difficulty in determining the correct place of therapeutic abortion. Comparing the incidence of therapeutic abortion and the maternal mortality rates of 2 British hospitals, 2 Irish hospitals and the Cape Town unit, no satisfactory conclusions can be drawn. Valvotomy is probably best done after termination, but it may be done during pregnancy. Therapeutic abortion has a very small place in the management of the cardiac patient. *L. J. Abramowitz*

151. **Fibrinogen-Fibrin Conversion Syndrome.**

By C. P. HODGKINSON. *West. J. Surg. Obstet. Gynec.*, **64**, 658–662. Dec. 1956.

This term is used in preference to afibrinogenaemia or hypofibrinogenaemia as it gives a clearer concept of the physio-pathological processes involved. The aetiological agent is thought to be thromboplastin and the essential mechanism is hyperthromboplastinaemia. Thromboplastin itself has not been isolated but its presence can be recognized by its property of increasing the coagulation of blood, any tissue extract contains it, and *in vivo* cell trauma incites its production. Fibrinogen is one of the three fractions of blood plasma protein and its normal concentration is 200–400 mg. per 100 ml. plasma. Its source of manufacture is the liver and disease of this organ decreases the plasma concentration; pregnancy, high protein diet and chronic infection increase its concentration. If liver function is normal, complete reconstitution of the plasma concentration can occur in 24 hours. When thromboplastin is liberated, fibrinogen is converted into an amorphous net-like gel which later shrinks and causes clot retraction. If the liberation of thromboplastin is precipitous and massive the symptoms produced are embolic, and because the pulmonary arterioles are mainly involved symptoms are mostly cardio-respiratory and manifest clinically as shock. When the process is less acute the circulating fibrinogen is gradually depleted and haemorrhage of uncoagulable blood may occur. Four general clinical types of the syndrome have been recognized: (1) The hyper-acute type is characterized by amniotic fluid embolism where death results from the intravenous infusion of thromboplastin-containing fluid; (2) The acute haemorrhagic-embolic type is seen in abruptio placentae, The symptomatology is usually mixed, with haemorrhage of uncoagulable blood predominating; (3) The chronic haemorrhagic type is seen in the "dead foetus syndrome". The onset is gradual and latent hypofibrinogenaemia may threaten for weeks before symptoms appear; (4) The delayed embolic type is associated with necrosis of the renal cortex, pituitary and adrenals after obstetric shock.

In addition to these overt clinical types a latent form has been recognized; by serial fibrinogen estimations in patients with abruptio placentae a falling concentration may be seen. Clinical symptoms may appear when the concentration drops to 150 mg. per 100 ml. plasma, and below the critical level of 90 mg. per 100 ml. spontaneous haemorrhage may occur. Diagnosis pre-supposes a knowledge of the basic physiology of the condition but laboratory tests are time-consuming and laborious. The best test for clinical use is the "clot observation test" of Weiner, Reid and Roby. Five ml. of blood are put in a dry test-tube about 8 mm. in diameter and the tube tilted at 2–4 minute intervals to observe clotting. Normal blood clots in 8–12 minutes and the clot remains intact for 24 hours. If no clot forms the fibrinogen concentration can be assumed to be less than 60 mg. per 100 ml.; if a filmy clot forms which undergoes dissolution in 20–30 minutes the concentration is below 100 mg. per 100 ml. Concentrations above this give progressively firmer and more stable clots. It is possible that tachycardia may be a useful sign of latent hypofibrinogenaemia but its importance as a warning sign remains to be proven. Treatment of the acute embolic type of syndrome is symptomatic; hypotension is best

treated by a long-acting sympathomimetic drug as care must be taken to avoid over-administration of parenteral fluid. Haemorrhage of uncoagulable blood is best treated by the intravenous administration of 8–12 grams of fibrinogen. In abruptio placentae the presence of shock should be taken as evidence of the syndrome and the restoration of blood volume or fibrinogen concentration effected by the administration of fresh whole blood and, if necessary, fibrinogen. The chronic haemorrhagic defibrination of the "dead foetus syndrome" should provoke a change in the usual conservative management of these cases and weekly fibrinogen estimations are essential. If the concentration falls below 150 mg./100 ml. active intervention should follow; at least 8 grams of fibrinogen should be available and fresh whole blood used in quantities sufficient to maintain an adequate circulating blood volume. The administration of fibrinogen carries a considerable risk of inoculation with the virus of infective hepatitis, and gammaglobulin in high dosage at 5-weekly intervals for 6 months has been advocated as a prophylactic. Treatment of the delayed embolic type depends on the organ affected.

[This is an excellent review of a most complicated and ill-understood subject.]

D. C. A. Bevis

152. **Pregnancy and Haemolytic Anaemia.** (Grossesse et anémie hémolytique.)

By C. WIRTHEIMER. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 651–660. 1956. 5 refs.

A 23-years-old secundipara was admitted in an alarming condition with an elevated temperature and a very low red cell count. The possibility of haemolytic anaemia was considered. After several transfusions a temporary remission occurred, but the foetus died and premature labour was induced. However, neither evacuation of the uterine contents, nor any form of treatment led to any improvement. The red cell count fell to 450,000 per cu.mm.

At this point, as there was no response, treatment was abandoned, yet the patient gradually made a complete recovery.

The diagnosis of haemolytic anaemia was confirmed by the appearance of an agglutinin in the blood, by the elevated reticulocytosis and by the study of the bone-marrow.

From the Author's Abstract

153. **Megaloblastic Anaemia of Pregnancy.**

By J. ADNO. *S. Afr. med. J.*, **31**, 10–15. Jan. 5, 1957. 10 tables. 24 refs.

The author has studied 7 cases of megaloblastic anaemia of pregnancy diagnosed antenatally at the Queen Victoria Maternity Hospital, Johannesburg. These were found in 7,500 antenatal cases.

In the majority of published series, quoted by the author, diagnosis has been late and in only a few cases was it made in the antenatal period. The mean age in 5 series was between 28·7 and 33 years, which is much lower than in Addisonian pernicious anaemia. Six of the 7 patients were multiparae, and 4 had had more than 5 pregnancies. Three patients had histamine-fast achlorhydria, 2 had hypochlorhydria and in 1 case free hydrochloric acid was present. The cases are reported in detail.

Folic acid seems to be the treatment of choice in megaloblastic anaemia of pregnancy during both the antenatal and post-partum periods. Controversial results have been reported with the use of vitamin B_{12}. Blood transfusion should be used when the haemoglobin level is to be restored hurriedly, as in cases near term, in threatening premature labour in the anaemic patient, or for patients actually in labour.

The author believes that haemoglobin estimations should be done at the patient's first visit to the doctor, and subsequently at monthly intervals. Patients with a haemoglobin of 11 g./100 ml. or less should be observed and certainly investigated if the level drops any farther, particularly while on iron supplements. Often macrocytes are not seen in the peripheral blood when a bone marrow examination is typical of megaloblastic anaemia. Correct therapy must be instituted early as the danger of premature labour, ante-, intra-, or post-partum haemorrhage may prove embarrassing to an anaemic patient.

L. J. Abramowitz

154. **Is the Birth of a "Giant Baby" a Symptom of Maternal Prediabetes?** (Ist die Geburt eines Riesenkindes Symptom eines mutterlichen Prädiabetes?)

By K. CRETIUS. *Gynaecologia, Basel*, **143**, 18–32. Jan. 1957. 2 tables, 71 refs.

The author discusses the literature on diabetic mothers, especially the reason for the large size of their babies, and the high foetal mortality. He became interested in determining whether mothers who produce excessively large babies (4,500 g. or more) tend to become diabetics.

From 1937 to 1952, there were 12,363 births at Universitäts-Frauenklinik, Mainz and 177 infants weighed 4,500 g. or more (1·4 per cent). He followed up 46 of these women, examining them 1½–17 years after the birth of their first excessively large baby. The examination included a glucose tolerance test. Five proved to be diabetics. Their average age at the time of the birth of the first "large baby" was 31·9 years, and the average for the 5 diabetics 34·8 years. At the follow-up examination the average age was 31·9; for the diabetics 42 years. Only 4 women were over 50 years old. The author considers the age important, because the incidence of diabetes is known to rise at the menopause.

The 46 women averaged 3·3 births and the perinatal mortality was surprisingly low. Out of 153 births there were 8 deaths within 10 days, including stillbirths.

In 10 the "large baby" was the result of a first pregnancy, in 16 the second, 7 the third, 5 the fourth, and 8 the fifth or more. Twelve of the 46 women had only one overweight baby, 8 two, 1 three and 3 four or more. Of the 5 diabetic women, 3 had more than one overweight baby. Ten of the 46 women gave a family history of diabetes but none of the diabetic women.

It proved impossible to determine the maternal

weight at the time of the birth of the overweight baby as the hospital records lacked details. At the follow-up examination 10 were definitely obese. This may not have been of significance as women over 40 tend to gain weight.

The author appreciates that the numbers are too small to draw conclusions. He was interested in the incidence of diabetes in the general population. In post-war Germany this has been stated to be about 1–6 per 1,000 and other European countries quote 2–3 per 1,000.

The author quotes the findings of other investigators: Kriss and Futscher found that 50 per cent of women giving birth to an overweight baby developed diabetes within 25 years. Kritzer examined 58 such mothers within 2½ years of the birth and 31 per cent were diabetics. Gilbert found 6 out of 21 after 6 years.

From his investigation the author is still doubtful whether an excessively large baby indicates maternal pre-diabetes.

Jean Hallum

155. **Diabetes in Pregnancy.**

By J. T. Louw and R. St.C. Sinclair. *S. Afr. med. J.*, **31**, 28–31. Jan. 12, 1957. 2 tables. 2 figs. 14 refs.

Great strides have been made in reducing the maternal mortality in pregnant diabetics, but the foetal loss is still high. Uncontrolled diabetes may depress genital function, and an illustrative case of this nature is described.

Effect of Pregnancy, Labour and Puerperium on Diabetes

Nausea and vomiting in the early months may affect the dietary control. With the drop in renal threshold from the fourth month onwards, control becomes difficult and large quantities of sugar are passed. Lactosuria may further complicate the picture. In the second and third trimesters the insulin requirement is raised in at least 75 per cent of cases. Often latent diabetes is shown up by pregnancy. The deterioration of carbohydrate tolerance may well be due to pituitary overactivity during pregnancy—its diabetogenic factor amongst others. Increased muscular activity in labour may result in hypoglycaemia and a sudden drop in insulin requirement. Diabetic control in prolonged labour is difficult. Immediately after delivery there is an improvement in carbohydrate tolerance, and the old balance is soon regained or a better one established.

Effect of Diabetes on Pregnancy and Labour

It was not the authors' experience that diabetes predisposed to abortion. Of 127 diabetics only 2 aborted spontaneously. There seems to be a higher incidence of hypertension and albuminuria, and the incidence of hydramnios is stated to be high. No statement can be made on prematurity, as pregnancy was terminated early. A large baby may give rise to complications in labour. There were no maternal deaths in the present series, but insulin therapy did not very markedly decrease the foetal mortality. The babies have an inherently poor vitality and should be treated as premature infants. It is very likely that the intra-uterine deaths and production of large babies are both due to the anterior pituitary, and the administration of stilboestrol and progesterone may depress this altered secretion. The Medical Research Council experiment in the United Kingdom does not however demonstrate decreased foetal mortality with hormone administration. It has been shown that congenital abnormalities can be produced by injecting insulin into developing chicks' eggs.

With regard to treatment, the diabetes must be controlled. If this proves difficult, the patient should be admitted to hospital. In any case she should be admitted from the 32nd week onwards. Pregnancy should be terminated soon after 36 weeks. If there is no response to induction or if labour is prolonged, Caesarean section should be performed. Treatment of the infant should be as for a premature baby with a good oxygen supply and a humid atmosphere. Gastric aspiration soon after delivery is an added precaution.

Of 90 booked cases 7 babies were stillborn and 7 died neonatally. This is a foetal loss of 15·5 per cent. In the unbooked cases the stillbirth rate was 41·2 per cent, and the combined foetal loss was 22·6 per cent. The foetal loss following Caesarean section was much lower (5·9 per cent) than that following vaginal delivery (34·3 per cent). The latter however included many cases of intra-uterine death. It is believed that the duration of adequate control during pregnancy is of vital importance to the foetus.

L. J. Abramowitz

156. **Hyperthyroidism in a Pregnant Diabetic.** (Hyperthyroïdie chez une femme enceinte diabétique.)

By R. Tagnon, A. Ghilain and R. Wolter. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 614–619. 1956.

A patient treated for serious diabetes and hypothyroidism was, after five and a half months gestation, delivered of a normal premature child, overweight, but with no fundamental somatic disorder or congenital anomaly. The intensive treatment with thyroid-depressing drugs in the second half of the pregnancy did not entail any hypothyroidism or goitre in the child.

From the Authors' Abstract

157. **Pregnancy in the Diabetic Mother with Nephritis.**

By T. E. Oppe, D. Yi-Yung Hsia and S. S. Gellis. *Lancet*, **1**, 353–354. Feb. 16, 1957. 2 tables. 6 refs.

The authors analyze the results of 41 pregnancies in diabetic women who also had chronic renal disease. All the expectant mothers had nitrogen retention and some had hypertension and diminished renal function. Of the 41 pregnancies, 2 ended in abortion, 8 in therapeutic abortion and 4 in stillbirth delivery. There were 27 live-born infants, 8 of whom died in the neonatal period. They conclude that the diabetic woman with nephritis has a 50 per cent chance of having a surviving child.

H. H. Fouracre Barns

158. **Vaccination and Virus Diseases During Pregnancy.**

By L. J. Abramowitz. *S. Afr. med. J.*, **31**, 1–3. Jan. 5, 1957. 2 tables. 25 refs.

There is controversy in the literature with regard to the effects of vaccination in early pregnancy. MacArthur

found a high incidence of abortions and stillbirths in patients vaccinated between the fourth and twelfth weeks of gestation. The author has studied the effects of vaccination on the stillbirth rate, the neonatal death rate and the congenital abnormality rate in 1,121 patients, and has compared this with 201 controls. Of the 1,121 patients, 510 had positive reactions and 611 had negative reactions. There were no significant differences in these groups.

Unfortunately, because of late booking, a forward type of investigation of the abortion rate could not be made. In 6 cases, however, with positive reactions seen between the fourth and twelfth weeks of gestation, all had normal babies, 1 being premature.

The controversial "congenital abnormality rates" due to rubella which have been published are discussed, as are the types of abnormality and the pathogenesis. The chief problems which arise in dealing with a case are:

(1) Did the patient actually have rubella?

(2) Should she be informed of the risks to which the foetus has been exposed?

(3) Should therapeutic abortion be performed?

Legally the only indication for termination is the psychiatric aspect. With free discussion in the lay press grave psychological states may be produced in pregnant women with rubella. Preventive measures include "Rubella camps", isolation and the administration of gamma globulin. In Australia a special gamma globulin is prepared from convalescent rubella patients.

The effects of measles, chicken-pox, herpes zoster, mumps, infective hepatitis, poliomyelitis and influenza on the foetal abnormality rate are discussed and tabled. Authorities quoted estimate that maternal rubella is responsible for 4–5 per cent of all congenital abnormalities.

Author's Abstract

159. **Pregnancy Following Contralateral Haematosalpinx Caused by Simultaneous Tubal Pregnancy.**

By P. A. Järvinen and O. Kinnunen. *Ann. chir. gynaec. fenn.*, **45**, 275–288. 1956. 9 refs.

In 1785 operations performed for ectopic gestation, contralateral haematosalpinx was found in 29 cases. In 19 of these both tubes were removed, but in the other 10 the haematosalpinx was treated conservatively by salpingostomy, salpingolysis, resection or "milking" the tube. Only one of these cases subsequently became pregnant, namely in that case where "milking" of the tube had been carried out. The authors discuss the aetiology of contralateral haematosalpinx and make a plea for conservative treatment, especially "milking" the tube, sometimes with polythene tube insertion.

D. M. Sheppard

160. **Preservation of Fertility by Conservative Surgery for Ectopic Pregnancy: Principles and Report of a Case.**

By P. Tompkins. *Fertil. Steril.*, **7**, 448–455. Sept.-Oct. 1956.

This surgeon is firmly convinced that salpingectomy for the unruptured tubal pregnancy, or the leaking ampullary ectopic should be discontinued, a line of thought with which many in this country would agree. He gently grasps the tubal pregnancy and incises it with a knife or sharp pointed scissors, and the ovum is evacuated with the handle of a knife. The bleeding is minimal, and if need be, diathermy can be used to control it, or the finest of fine catgut. After the conceptus is removed no attempt is made to close the tube. This also holds good if he slits up the tube from the fimbriated end, provided of course that there is no actual bleeding from the cut surfaces, which he states rarely occurs. Free blood is not evacuated though clots are lifted out with the hand. His cases have been followed up by salpingograms and none of those on whom this was done showed any abnormality in the tube that was operated upon, though two patients had recurrent ectopic pregnancies in the other tube.

[The author does not like sponges or suction to remove liquid blood, nor does he speak of ventro-suspension with one catgut suture before closing the abdomen. Otherwise many will agree with his technique.]

V. B. Green-Armytage

161. **Secondary Abdominal Pregnancy: Report of a Case in a Bantu Female.**

By J. L. Smith and E. C. Newborn. *S. Afr. med. J.*, **30**, 1245–1246. Dec. 30, 1956. 1 ref.

The authors present the case of a 34-year-old Bantu woman with a 16-week secondary abdominal pregnancy. She was admitted in an anaemic state with a temperature of 102° F. and a dark brown haemorrhagic vaginal discharge. Following restorative and antibiotic therapy the patient's condition improved and a mass was palpated which was separate from the uterus. Laparotomy revealed an extra-uterine pregnancy. The pathology and the clinical features of the condition are discussed and the difficulty in diagnosis is stressed.

L. J. Abramowitz

162. **Nine Cases of Abdominal Pregnancy at Term with One Living Child.** (Présentation de 9 grossesses abdominales à terme avec un enfant vivant.)

By M. Crest. *Gynéc. Obstét.*, **55**, 427–434. 1956.

Amongst the 9 cases, 1 developed in the right ovary, but the other 8 cases were secondary abdominal pregnancies following tubal rupture (5 from the left side and 3 from the right). Seven of these cases were operated on between 2 and 4 months after the foetus had died. Two were operated on at term and 1 of these had a living child. In this case a dissection of the sac was carried out. In 5 patients the sacs were marsupialized with obliteration 1–3 months later. The last method seems to the writer to be the simplest and the least shocking technique.

The author insists on the ease of diagnosis and on the importance of taking action as soon as false labour starts, and doing the minimal amount of surgery (marsupialization or obliteration of the sac). None of the 9 foetuses showed the malformation described in the literature, and the living child developed quite normally.

D. Maxwell

LABOUR

163. Observations on Psychological Preparation for Labour in Private Practice. (Considérations sur la méthode psycho-prophylactique de l'accouchement en clientèle privée.)

By G. DE WERRA and P. DUBUIS. *Gynaecologia, Basel*, **142**, 357–360. Nov. 1956. 2 tables.

The authors decided to prepare 164 out of 246 women, i.e., 66 per cent, but 90 per cent attended.

The results are tabulated and show that:

(1) The newborn infants seldom required resuscitation (in 1·2 per cent) and the paediatricians were greatly impressed.

(2) The length of the second stage of labour was reduced, averaging 39 minutes in primigravidae.

(3) Forceps deliveries were less frequent, although necessary for mechanical and foetal indications. However, it was possible to apply forceps painlessly, under narcosis.

(4) There were fewer first degree perineal tears and none of second or third degree. The tears occurred mainly in multiparae when the perineum was already scarred and friable.

(5) There was slight shortening of the first stage of labour.

(6) The best results were when the patient reached the clinic in labour with the cervix dilated to 2–5 francs.

The authors admit that psychological results are difficult to assess, but maintain it is possible to observe the presence or absence of pain in patients whom they know and who have been taught not to suppress sensations. Their results are divided into excellent, very good, average and failures—36·8 per cent of the primigravidae came into the first group and 5·7 per cent into the last. Multiparae gave slightly better results. The authors consider these results are comparable to others using similar methods of preparation. They discuss the cause of failures, separating them into physical and psychological.

They found that 46 per cent primigravidae and 21 per cent multiparae had lumbar pain during pregnancy due, as Burthiault and Garnier suggest, to excessive relaxation of the lumbar vertebrae with disc displacement. Some with this pain lost it when labour commenced but in others it persisted and did not respond well even to analgesic and antispasmodic drugs.

They found that labours induced by oxytocic drugs caused unphysiological and painful contractions. This was also true with a hypertonic uterus and spastic cervix. An unduly prolonged labour in a primigravida often caused failure.

Postmaturity was associated with failure as the woman often worried in case the baby would be excessively large. Premature rupture of membranes, especially when the patient lay in bed for some time at the clinic, was another cause. Equally, patients who only reached the clinic in the second stage of labour did not have time to adjust themselves.

Premature labours gave psychological failures as the patient doubted if the infant would survive, and also might not have completed the preparatory course.

In multiparae failures were often associated with previous difficult labours and fear of their recurrence. Prolonged sterility and previous stillbirths or abortions were other causes.

Semi-failures were probably most often due to an inadequate number of trained staff, meaning that sometimes the patient had to be left for a time in labour. In addition the method of preparation used was uniform but should undoubtedly be adjusted to each individual nervous type of patient. The authors believe the method is good and failures encourage them to alter and adapt their methods.

Jean Hallum

164. Treatment of Uterine Inertia with Intravenous Pitocin Drip.

By M. P. JOHN and S. PANDEY. *J. Obstet. Gynaec. India*, **7**, 95–100. Dec. 1956. 9 refs.

This is a brief article describing the authors' experience of the pitocin drip. Twenty-eight cases were treated in all. Cases were selected of "uterine inertia due to weak contractions". Disproportion and malpresentations were ruled out, and very multiparous women were excluded.

The technique was to employ 5 units of pitocin in 500 c.c. of 5 per cent glucose. It was run in at 10 drops per minute, increasing gradually to 50 drops per minute, depending on the response of the uterine muscle. The length of each labour before and after the pitocin drip is tabulated.

Improvement in the character of the labours occurred within 3 or 4 minutes of starting the drip in most cases. The response to the drip bore no relation to the degree of cervical dilatation when the drip was started, nor was the response related to the state of the membranes. The drip was continued well after the third stage, which lasted, on an average, four minutes, and the average amount of pitocin used was 2·5 units per case. There were no foetal deaths which could be attributed to the drug.

It is concluded from this small series that the intravenous pitocin drip is a safe and efficient method of stimulating weak uterine contractions in selected cases, and that it thereby helps to reduce intra-partum infection, difficult forceps deliveries, and the number of Caesarean sections.

John McKiddie

165. Induction of Labour to Prevent Recurrent Stillbirth Due to Haemolytic Disease.

By W. WALKER, S. MURRAY and J. K. RUSSELL. *Lancet*, **1**, 348–350. Feb. 16, 1957. 4 tables. 1 fig. 14 refs.

The overall risk of stillbirth in haemolytic disease varies from 2 per cent following mild disease in a previous pregnancy to 80 per cent following multiple stillbirths. The authors made a trial of premature induction of labour in families in which a previous stillbirth had been due to haemolytic disease and in which the father was homozygous D/D. Labour was induced 35 days before the expected date of delivery. Sixty mothers were selected but only 25 reached 35 weeks with a living foetus apparently normal on X-ray examination. The authors conclude that if there has been a previous stillbirth due

to haemolytic disease and a subsequent Rh-positive foetus reaches 35 weeks gestation alive and not hydropic on X-ray examination, premature induction at this stage gives a better chance of live birth than does spontaneous delivery. Relatively severe disease is to be expected in any liveborn baby if a previous sibling was stillborn with haemolytic disease and arrangements must be made for prompt exchange transfusion treatment. Some premature babies unfortunately tolerate exchange transfusion badly.

H. H. Fouracre Barns

166. **The Fixation Effects of Uterine Ligaments During Labour.** (Zur Ligamentverankerung des Uterus sub partu.)

By W. LANGREDER. *Zbl. Gynäk.*, **79**, 19–29. Jan. 5, 1957. 6 figs. 43 refs.

In this paper the views of G. Narik regarding the mechanism of labour are subjected to detailed criticism. Narik recently disputed the anchoring effect of the parametrial ligaments of the uterus in labour. (The papers referred to are: *Zbl. Gynäk.*, 1951, **73**, 1262; *Geburtsh. u. Frauenheilk.*, 1955, **5**, 402; *Geburtsh. u. Frauenheilk.*, 1956, **6**, 530.) The author's main arguments against this view are as follows.

During Caesarean section in labour direct palpation reveals the increased tension in the parametrial tissues on the sides of the cervix. This results partly from the pull of uterine contractions.

If the cervix was not fixed it would be withdrawn cranially over the presenting part of the foetus. As the os dilates from 1 cm. to about 34 cm. during the first stage, the parametrial fibres are spread apart, the whole parametrium is shortened and tends to pull the uterus downwards.

There is little doubt that the portio descends during labour, partly due to the propulsion by the foetus, and partly owing to the pull of the parametrium.

In cases of disproportion and cervical rigidity, the smooth muscle in the region of the isthmus or the parametrium will be strained. If the uterus is unable to overcome the obstruction, tears will result in the region of the birth canal and its surrounding supports.

Narik considered the parametrial fibrous tracts too weak (microscopically and macroscopically) to be able to fix the cervix. The author demonstrated convincingly the strength of these structures in cadaveric specimens from women who had died in labour. The importance of the ligamentous supports is also indicated by their considerable hypertrophy during pregnancy, reaching a maximum towards term.

The isthmus, too, is stronger than Narik believes, as it is capable of withstanding the two-way pull of the corpus and the parametrium. It can tolerate considerable tension, as seen clinically in cases of impacted shoulder.

The author dismisses Narik's view that the uterus in labour is fixed by the round ligaments, rather than the parametrium. He also disproved by measurements Narik's claim that the level of the fundus does not descend during labour.

Bruce Eton

167. **Obstetrical Haemorrhagic Syndrome Associated with Defects in Blood Coagulation Due to Defibrination.** (Les syndromes hémorragiques obstétricaux avec défaut de coagulation du sang par défibrination.)

By M. LEROUX. *Gynéc. Obstét.*, **55**, 357–381. 1956. 114 refs.

This is a satisfactory review of the present knowledge on this subject which includes a list of 114 references and reports on 9 specific cases from the Nantes area. As regards aetiology the writer divides the cases into 4 groups:

(*a*) Those in which there is premature separation of the placenta.
(*b*) Those with retention of a dead ovum.
(*c*) Those with amniotic emboli.
(*d*) A few cases are unexplained.

In cases of post-partum haemorrhage when blood remains unclotted defibrination may be suspected. This sign must, however, be supported by the search for ecchymoses, purpuric spots, subcutaneous or submucous haemorrhages. In addition the diagnosis must also be substantiated by examination of blood taken from a vein, which will remain uncoagulated at blood temperature, or if a clot does form it re-dissolves in 30 to 60 minutes.

The writer elaborates the 3 usually recognized theories about this disorder, namely the hepatic theory, the thromboplastin theory, and that of fibrinolysis (or better proteolysis).

For treatment he stresses the value of human fibrinogen and alludes to Weiner's figures when 34 cases were reported with 34 cures.

Fibrinogen is manufactured in France according to the technique of Cohn. The price in France at the time of going to press was 5,400 francs per gramme. About 10 minutes after the beginning of treatment the blood ceases to flow, and clots form. Whole blood should also be used to re-establish blood volume in order to prevent reversion to shock and vascular collapse. In some mild cases of this condition, in the writer's opinion, blood alone will suffice to cure. Plasma can be employed immediately the diagnosis is made without any grouping of blood and may be very valuable while waiting for blood and is usually easily obtainable. This substance acts in retaining the level of blood proteins. Additional drugs in the form of oxygen, intravenous calcium, morphia and atropine may all be useful.

Hysterectomy is only advised in those rare cases where the uterus already emptied of its contents does not regain its normal contractility.

In cases occurring prior to evacuation of the uterus, rupture of the membranes is advised in order to minimize tension within the ovum and to favour dilatation of the cervix. If labour is prolonged or if the general state of the patient worsens, vaginal delivery may have to be abandoned in favour of abdominal hysterotomy.

D. Maxwell

168. **Caudal Analgesia in Obstetrics. Report of Thirteen Years' Experience.**

By L. F. RITMILLER and E. T. RIPPMANN. *Obstet. Gynec.*, **9**, 25–28. Jan. 1957. 5 tables. 2 refs.

In the years 1943–1956, 9,534 patients out of a total of 11,178 vaginal deliveries were given either single dose or continuous caudal analgesia at the George Geisinger Memorial Hospital, Danville, Pennsylvania. One and a half per cent metycaine solution was used. The authors believe that this method is ideally suited to obstetrics, perfectly safe and very satisfactory, but success depends on perfect mastery of the technique.

The method prolonged labour by 1 hour on the average in the primigravida and 2 hours in the multipara. Correct timing of the injection is necessary: it should not be given too soon but it can be prolonged for 6–10 hours. Analgesia is commenced in the primigravida in the late first or early second stage, and at 8–9 cm. dilatation in the multipara.

Contra-indications to caudal analgesia include antepartum haemorrhage, sensitivity to the analgesic agent, diseases of the central nervous system, local infection at the site of injection, and subarachnoid puncture with the caudal needle.

Spontaneous delivery occurred in 44 per cent of cases, and forceps in 52 per cent, the remainder being breech deliveries.

J. G. Dumoulin

169. **Spinal Anesthesia in More than Thirty-Four Thousand Vaginal Deliveries.**

By G. A. Macer. *West. J. Surg. Obstet. Gynec.*, **64**, 625–629. Dec. 1956. 13 refs.

The author reviews the results of 34,936 vaginal deliveries in two hospitals from 1943 to 1955. One hospital employed only qualified specialists while the other was a general practitioner unit. The total number of deliveries in the period was 50,898 and cases requiring Caesarean section are not considered as the anaesthetic in these cases was usually given by a specialized anaesthetist. The technique used is considered to be important. The patient is pre-medicated with a barbiturate and placed on her side with the head raised 2–3 inches, a hyperbaric solution of 5–6 mg. pontocaine in 1·5–2·0 ml. of 10 per cent glucose is injected through a 20 or 22 gauge needle into the 4th or 5th lumbar interspace, no spinal fluid is withdrawn and the injection is made slowly (5–10 seconds). The patient is immediately placed on her back and the table levelled, a pillow being placed under the head. Anaesthesia reaches the 12th thoracic segment but the level is easily controlled by tilting the table. The drug is usually given when delivery is expected within an hour. Results have been uniformly good, there were no anaesthetic deaths and no serious neurological symptoms. Hypotension was noted in less than half a dozen cases and is thought to be due to rapid injection. Headache was noted in about 10 per cent of the cases and required symptomatic treatment with analgesics, tight abdominal binders and bed-rest. Meningism was noted in a few cases and was due to intradural extravasation of blood. The method appears to be very safe.

D. C. A. Bevis

PUERPERIUM

170. **Puerperal Thrombosis.** (La trombofilia del puerperio.)

By U. Ciulla. *Ann. Ostet. Ginec.*, **78**, 383–394. 1956. 4 figs. 51 refs.

The factors which lead to hyper-coagulability of the blood in the early days of the puerperium, that is before the eleventh to twelfth day, are discussed. These factors include increased fibrinogen, prothrombin and Factor VII, accompanied by a numerical increase in the number of platelets and an increase in the agglutinability of these platelets. There is also a tendency to increased coagulability of the red blood cells. At the same time there is a reduction in a substance resembling heparin found in the blood during the latter part of pregnancy and also a reduction in fibrinolytic activity, which is raised during labour and delivery. A combination of these factors leads inevitably to a tendency towards thrombosis in the puerperium.

Josephine Barnes

171. **Post-partum Pituitary and Renal Necrosis: Case Report and Discussion of Pathogenesis of Post-partum Necrosis of the Anterior Lobe of the Pituitary Gland Associated with Acute Renal Tubular Necrosis.**

By D. Magner, P. N. Karnauchow, H. R. de Saint Victor and R. K. Smiley. *Obstet. Gynec.*, **9**, 77–85. Jan. 1957. 5 figs. 29 refs.

The authors report a case of traumatic rupture of the uterus during delivery who became profoundly shocked whilst undergoing hysterectomy and died 7 days post-partum. Autopsy revealed post-partum necrosis of the anterior lobe of the pituitary gland associated with acute renal tubular necrosis. The aetiological factors in the causation of these lesions are discussed and the view put forward that both were due to simple anoxia associated with shock in the absence of a primary vascular lesion.

J. G. Dumoulin

172. **Local Treatment of Chronic Nasal Carriers of *Staphylococcus aureus* with Tetracyclin and Mixed Vaccine.** (Behandlung chronischer Staphylokokkenträger mit Tetrazyklin- und Antipiolnasensalbe.)

By M. Breuning. *Zbl. Gynäk.*, **79**, 29–32. Jan. 5, 1957. 2 tables. 18 refs.

This is an account of an attempt to reduce the incidence of puerperal and neonatal infections due to drug-resistant staphylococci in hospitals.

The carrier rate amongst the nursing staff in institutions in and around Leipzig varied between 25 and 70 per cent.

One group of 43 carriers was supplied with nasal ointment containing vaccine (sterile filtrates of streptococci, staphylococci, *Ps. pyocyanea* and *E. coli*). The treatment was entirely successful in 19, moderately successful in 17 and failed in 7 cases.

Another group of 43 carriers was given 1 per cent tetracyclin ointment. This was entirely successful in 13, moderately successful in 20 and failed in 10 cases.

A further group of 17 was treated with both ointments

with an interval of 2 weeks. The two preparations gave equally good results in 5 cases; in 5 tetracyclin was more efficient and in 7 the vaccine.

Although the author admits that the presence of staphylococcal carriers is not the only factor on which the incidence of breast infection depends, he was able to observe at the Women's Clinic of the University of Leipzig that the reduction of carriers was followed by a decrease in the incidence of mastitis from 12·1 per cent to 4·5 per cent within one year and to 2·1 per cent by the second year.

Bruce Eton

OBSTETRIC OPERATIONS

173. **Change in the Frequency of Abdominal Caesarean Section During the Last Three Years (1953–1955) in the Maternity Department of the Hôpital Universitaire St-Pierre, Brussels.** (Considérations sur l'évolution de la fréquence de la césarienne abdominale au cours des trois dernières années (1953–1955) à la Maternité de l'Hôpital Universitaire St-Pierre, à Bruxelles.)

By P. Piraux. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 661–674. 1956. 2 tables. 1 fig.

During the last three years (1953–1955) at the Maternity Clinic many fewer Caesarean sections were performed, constituting only 1 per cent of all deliveries.

The change is justified by an improvement in the general results, with a decreased total of operative deliveries, reduction of total and pyrexial maternal morbidity, and a reduction of the corrected foetal mortality figures. In the course of these three years it was possible to avoid some seventy Caesarean sections.

From the Author's Abstract

174. **Foetal Mortality in Caesarean Section.**

By M. Grossman and R. C. Benson. *J. Amer. med. Ass.*, **162**, 1289–1293. Dec. 1, 1956. 5 refs.

After reviewing the results of Caesarean section for the past 48 years at the University of California Medical Centre in San Francisco, the authors examine in detail the perinatal mortality over the last 16 years (1940–1955). During this period 569 Caesarean sections were performed with a gross foetal mortality of 8·2 per cent. After allowance for congenital abnormalities, known non-viable babies, erythroblastotic infants, and those known to have died *in utero* before or during the operation, the corrected mortality was 2·9 per cent.

The two outstanding causes of mortality were: (1) prematurity, and (2) depression of the foetal respiratory centre brought on by hypoxia or toxic states of the mother. Prematurity is frequently unavoidable when immediate delivery is called for during some obstetric catastrophe, such as massive haemorrhage. There is, however, a smaller group where an error of dates or a misjudgment of foetal size results in a premature delivery by elective section. Premature separation of the placenta and placenta praevia are common causes of hypoxia in the foetus and the toxic state of the mother is often a contributory factor. Good regional anaesthesia, avoidance of oxygen lack before and during Caesarean section, and recognition by the paediatrician of the true nature of the problem during resuscitation are all important factors in reducing foetal loss.

D. W. James

175. **Labour Following Previous Caesarean Section.**

By M. R. Narvekar. *J. Obstet. Gynaec. India*, **7**, 115–133. Dec. 1956. 15 refs.

This is an essay on the changing attitude in India to the treatment of patients who have had one or more previous Caesarean sections. The most difficult cases are the ones in which the indication which necessitated the first section no longer exists, and the ones in which disproportion was the original indication. A history of disproportion can be misleading as it may be complicated by inefficient uterine action and an occipito-posterior position. There is often difficulty too, in assessing what constituted an adequate trial of the labour which ended in the previous section. Moreover, anxiety about the condition of the foetus may cause a trial labour to end by abdominal section more rapidly than it otherwise might.

Difficulty lies also in evaluation of a previous scar. Experimentally, the tensile strength of a scar may be greater than that of uninjured muscle, and interrupted sutures are thought to cause sounder healing than a continuous stitch. The type of suture material is unrelated to the strength of a scar, but a febrile convalescence may weaken it if the fever is due to uterine infection. It may be that scars are better if operation is performed after the lower segment is stretched, as an elective scar is more likely to be situated in the upper segment. Scars may be affected also by the undue stretching of hydramnios, or by softening due to placental implant over their site, and it is concluded that there is no certain criterion by which one can evaluate their strength.

If a patient has had two previous sections, it is usual to subject her to a third, especially as in such cases, the original indication usually persists. The type of previous operation may influence subsequent delivery, and it is thought that the maternal mortality from upper segment scar rupture is not much more than would be expected from a repeat section. The history of a vaginal delivery before or after a previous section is one of the most helpful factors in assessing the likely outcome of a subsequent labour.

The outcome of 55 repeat Caesarean sections is tabulated, and the reasons for vaginal or abdominal delivery are detailed. It is thought that if a vaginal delivery is achieved, routine manual exploration of the lower segment is a wise precaution.

John McKiddie

176. **Frequent Application of Forceps Does Not Improve Perinatal Mortality.** (Les applications fréquentes de forceps n'améliorent pas la mortalité périnatale.)

By F. Op de Beeck. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 721–729. 1956. 11 tables.

After discussing the statistical interpretation of obstetrical data generally, and in particular of those pertaining to forceps applications, the author compares

the results obtained in two clinics with different obstetrical attitude. He demonstrates that frequent forceps applications do not improve perinatal foetal mortality.

Author's Abstract

INFANT

177. **The Diagnosis of Fetal Sex During Pregnancy.**
By D. M. Serr, L. Sachs and M. Danon. *Surg. Gynec. Obstet.*, **104**, 157–162. Feb. 1957. 1 fig. 33 refs.

This report comes from the Rothschild Hadassah University Hospital, Jerusalem. The authors have previously shown that a reliable diagnosis of sex can be made before birth by the study of the chromocentres in cells in the amniotic fluid. They now discuss the method of obtaining the fluid, its practicability and the results obtained.

Fifty patients were examined in the 9th month of pregnancy. In most of these cases the fluid was obtained per vaginam by inserting a fine needle through the membranes prior to induction of labour, or during labour. In a number the needle was inserted through the uterine wall during Caesarean section and in one case of hydramnios the fluid was obtained by abdominal paracentesis performed for therapeutic reasons.

Thirteen patients were examined in the early months of pregnancy. In 2 the fluid was obtained following abortion or hysterectomy but in the remaining 11 abdominal paracentesis was performed between the 4th and 7th month of pregnancy. This was preceded by soft tissue radiography to ascertain as far as possible the position of the placenta.

In the 63 cases examined the diagnosis of foetal sex proved correct in all but one—an abnormal pregnancy in which insufficient cells were found. In no case did the paracentesis have an ill-effect on the pregnancy.

The authors discuss the possible complications of the test and consider that at the present time it should be reserved for the rare case in which the diagnosis of the sex of the embryo would enable the antenatal detection of a sex-linked hereditary disorder. They also suggest that blood grouping from epithelial cells and its possible application to the foetus *in utero* may give added importance to the test.

John P. Erskine

178. **Meconium Staining of the Amniotic Fluid: A Marker of Fetal Hypoxia.**
By M. M. Desmond, J. Moore, J. E. Lindley and C. A. Brown. *Obstet. Gynec.*, **9**, 91–103. Jan. 1957. 7 tables. 3 figs. 16 refs.

Green, yellow or meconium-stained fluid was found in 9·6 per cent of 3,965 deliveries. This condition is associated with an increase in neonatal mortality and morbidity. It is present predominantly at the delivery of term infants. Factors associated with its presence are increasing maternal age, a greater number of previous reproductive casualties, and an increased number of obstetric complications. These complications include obesity, toxaemia, anaemia and prolonged gestation.

Of the infants, 77·2 per cent had no difficulty at birth or in the neonatal period, 3·7 expired, 1·5 per cent had apnoea neonatorum, and 9·3 per cent had spontaneous onset of respiration with a variety of later neonatal difficulties.

J. G. Dumoulin

179. **Plasma Protein and NPN-Content of Maternal and Cord Blood.**
By N. Hallman, K. Österlund and P. Vara. *Ann. chir. gynaec. fenn.*, **45**, 270–274. 1956. 20 refs.

In 36 healthy women blood samples were taken from the maternal veins immediately before delivery and as soon as labour was completed. Blood was also taken from the umbilical artery and vein as soon as possible. Plasma proteins from the cord vessels were studied in 36 cases and from maternal blood in 31 cases by the Klingmüller modification of the micro-Kjeldahl method. Non-protein nitrogen was estimated by the Kjeldahl-Parnas method in blood from cord vessels in 16 cases and in maternal venous blood in 14 cases. All estimations were duplicated. No significant change could be found in maternal plasma proteins or NPN during the course of labour. Plasma proteins in cord blood were in significantly lower concentration than in maternal blood. There was no difference as regards maternal artery or vein. NPN in the umbilical artery was significantly greater than in the vein, and the authors state that maternal venous NPN was significantly greater than that of the venous value for the child.

[Their table, however, seems to indicate that the reverse was true.]

D. M. Sheppard

180. **Neonatal Blood Pressure in Relation to Maturity, Mode of Delivery and Condition at Birth.**
By W. W. Holland and I. M. Young. *Brit. med. J.*, **2**, 1331–1333. Dec. 8, 1956. 2 tables. 3 figs. 11 refs.

Systolic blood pressure measurements were made within an hour of birth and subsequently at intervals up to six months by palpating the brachial artery (in the antecubital fossa) below a 2·5 cm. inflatable cuff.

The normal mean systolic pressure was found to be 69 mm. Hg at birth and 93 mm. Hg at 6 months. Premature babies had a lower systolic pressure than full term infants. The difference was related to weight but not to maturity. By the third month measurements were not significantly different from those of full-term infants at the same stage.

Pre-eclampsia had no effect on neonatal systolic pressure at birth but a significant lowering of pressure was found to be associated with abnormal forms of delivery such as Caesarean section and also with foetal anoxia. In these cases, however, recovery to normal occurred within a few days.

The administration of such drugs as morphine, pethidine and barbiturates did not influence the values obtained.

R. W. Grayburn

GYNAECOLOGY

181. **The Diagnostic Value of Alkaline Glycerophosphatase in Microscopy.** (Valor diagnóstico de la glicerofosfatasa alcalina en el microlegrado.)

By J. Botella Llusiá. *Obstet. Ginec. lat.-amer.*, **14**, 59–63. Mar.–Apr. 1956. 6 figs. 13 refs.

Gomori, in 1941, introduced a histochemical method for testing for the enzyme glycerophosphatase in tissues. Other workers later applied his technique to the examination of animal and human endometrium.

By examining the endometrium at various stages in the menstrual cycle, investigators established the following facts: In the first week of the cycle, alkaline glycerophosphatase is present in the endometrial glands throughout the thickness of the cells, making them stand out against the stroma. In the second week, deposits are similar, but as the glands reach greater development, coloration is more intense. In the third week, the deposits begin to disappear leaving the cellular protoplasm free, but on the other hand the enzyme is deposited in the gland lumen. In the fourth week, the enzyme has totally disappeared from the glands, but may be present in the walls of the endometrial vessels. This substance is found in the endothelium of new vessels, a fact that explains its presence in pre-menstrual endometrium.

Using this method for microscopical study, the secretory phase of the menstrual cycle is characterized in the endometrium by depletion of the alkaline glycerophosphatase in the glands, its deposit in their lumen, and its presence in the vessel walls. If none is observed on the 24th–26th days of the cycle in the vessels, it is inferred that ovulation has not occurred. Lutein insufficiency is indicated by late beginning of secretion characteristics. Endometrial hyperplasia shows strong staining in the cells of the endometrial glands, lack of gland depletion and lack of staining in the endothelial cells of blood vessels. This test is therefore of value in diagnosing post-climacteric hyperplasia, and also irregular maturing of the endometrium, as well as other abnormalities—"menstrual abortions", etc.

The author concludes his article by stating that he is extending his research work with this method of investigation into tubercular infected endometrium.

[The stain used for identifying alkaline glycerophosphatase is not stated.]

John F. Foulkes

182. **Idiopathic Pelvic Neuralgia in Women.** (La névralgie pelvienne féminine essentielle.)

By P. Funck-Brentano. *Gynéc. Obstét.*, **55**, 341–356. 1956. 9 refs.

This paper by the Professor at the Broca Hospital, Paris includes reference to much of the work of his colleagues.

In introducing the subject he alludes to the persistent pain of carcinoma in the pelvis, the temporary pain of salpingitis, and the periodic pre-menstrual pain seen sometimes in cases of retroflexion, cervical canal obstruction or infantile uterus. The pain associated with cystic ovaries, which have often been operated on by means of partial oöphorectomy or oöphoropexy is more complex, and in these cases recurrent pain is sometimes relieved by psychotherapy or hormone therapy.

In certain cases, hydrosalpingography and coelioscopy may assist in excluding organic disease, and the importance of excluding extragenital causes is also stressed, for example chronic appendicitis, colitis, and diverticulitis. Geisendorf of Geneva has suggested that pelvic pain may be due to pelvic arthropathy, arthritis, disc lesions or sacro-iliac strain.

Pelvic pain is classified into *organic*, *functional* (including (*a*) dysmenorrhoea, (*b*) intermenstrual), and *idiopathic*. The onset of the last category may synchronize with puberty, the first act of intercourse, a miscarriage, a confinement or the menopause or some form of surgical gynaecological intervention.

Topography and Character of Pelvic Pain

It may be very difficult for the patient to state the precise position and quality of her pain. The pain may indeed be an excuse by which the patient introduces herself, and through it the real underlying reason for the consultation is divulged. With absence of any anatomical gynaecological lesion, it is essential to seek with the greatest care for possible extragenital causes, such as those in bowel, joints, and spine. Finally the psychological stability and neurotic capacity of the patient should be assessed.

The peripheral distribution of the patient's pain to certain skin areas may have considerable bearing in defining the gynaecological origin of the symptom. These areas include ventral and dorsal areas and the anterior surface of the thighs.

Deep tenderness may be present and is best exhibited by rectal rather than vaginal examination of the uterosacral ligaments. Associated symptoms from the bladder or bowel may assist in the diagnosis, in which case endoscopic examination may reveal their cause.

Treatment

In the absence of any organic signs, the gynaecologist must not yield to the temptation of laparotomy. The easy policy of "having a look" is not only useless but may be harmful. Therapy should be mainly psychological; as Mathieu and Cotte of Lyons put it in 1950—"We consider that it is essentially in gynaecology that primitive psychopathic disorders can be at their worst and for this reason we hold that often it is enough to remove the small 'irritating thorn' of organic element which is basically the origin, in order that the patient's psyche may recover its equilibrium completely."

(I) *Medical methods* include aspirin derivatives, antispasmodics and papaverine. Barbiturates and opium derivatives may lead to addiction.
(II) *Massage.*
(III) *Hydrotherapy.*
(IV) *Reflex therapy*, which is a modified form of acupuncture where multiple subcutaneous and intradermal injections may be used.

(V) *Physiotherapy*, including short-wave pelvic diathermy, ionization, and infra-red rays, and ultrasonic rays.

(VI) *Psychotherapy*. The author deals with this at some length in an analytical way.

(VII) *Surgery* is only employed with reluctance. Paracervical injections of novocaine by the vaginal route are not used for all cases. Pre-sacral neurectomy is carried out only after all other forms of therapy have failed, and when a careful assessment of the psychological state of the patient has been made. This must be a wide resection and may well be combined with peri-arterial sympathectomy of the internal iliac arteries.

The operation of George Roux may also be tried, this includes hysteropexy, pre-sacral neurectomy, and obliteration of the whole of the true pelvis. Total hysterectomy should only be carried out when all other methods have failed.

Of 57 intractable cases the writer had 71 per cent excellent results and 8 per cent reasonable results by total hysterectomy.

[The writer's command of language is outstanding and he bases his conclusions on a vast experience.]

D. Maxwell

183. **The Correlation Between Urinary Oestrogen and Vaginal Cytology.**

By S. Young, R. D. Bulbrook and F. C. Greenward. *Lancet*, **1**, 350–353. Feb. 16, 1957. 2 tables. 2 figs. 6 refs.

The authors report an attempt to determine the association between the level of oestrogens in the urine and the degree of oestrogen stimulation of the vaginal mucosa as judged by vaginal cytology in 53 women on 70 occasions. Good correlation was found, the best being given by oestriol which the authors suggest might be the end product of oestradiol and oestrone.

H. H. Fouracre Barns

184. **Methyloestrenolone, A New Progestogenic Substance** (La méthyloestrénolone, nouvelle substance progestogène.)

By J. Ferin. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 702–708. 1956. 10 refs.

Methyloestrenolone, or 17-methyl-19-nor-testosterone, is a progestogenic substance. By sublingual administration its activity is definitely superior to that of intramuscular progesterone.

From the Author's Abstract

185. **Comparative Clinical Study of Methyloestrenolone and Progesterone Administered Parenterally.** (Etude clinique comparative de la méthyloestrénolone et de la progestérone administrées par voie parentérale.)

By A. E. G. Fanard and A. Ghilain. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 709–720. 1956. 7 figs. 5 refs.

The authors observed that methyloestrenolone, given orally as well as by intramuscular injection, was able to provoke uterine bleeding in women subjected to continuous oestrogenic action.

They also compared the activity of parenterally administered methyloestrenolone and progesterone and determined the minimal dose required to produce "withdrawal bleeding".

The hormones were given under the same experimental conditions in two cases of secondary amenorrhoea, subjected to continuous oestrogenic administration. It appeared that in these conditions at least 25 mg. of progesterone and from 2 to 4 mg. of methyloestrenolone were required to produce withdrawal bleeding.

From the Authors' Abstract

186. **The Use of Tranquillizing Drugs in Gynecology.**

By R. H. Stewart. *West. J. Surg. Obstet. Gynec.*, **64**, 650–657. Dec. 1956. 18 refs. 2 figs.

The author discusses the role of the autonomic nervous system and Selye's "stress" hypothesis in the production of such gynaecological symptoms as dysmenorrhoea, pelvic congestion and menopausal flushing. He reports the successful use of a mixture of bellafoline (a parasympathetic depressant) and ergotamine (a sympathetic depressant) put on the market as "Bellergal". It is pointed out that in addition to the drugs used, the physician must approach the emotional problems which are the basic cause of the patient's complaint.

D. C. A. Bevis

187. **The Pathogenesis and Treatment of Premenstrual Tension.** (Moderni orientamenti in tema di etiopatogenesi e terapia della tensione premestruale.)

By C. Luraschi. *Ann. Ostet. Ginec.*, **78**, 421–430. 1956. 1 table. 84 refs.

The syndrome known as "premenstrual tension" is described. There are four main components, painful congestion of the breasts, abdomino-pelvic congestion, nervous lability and menstrual abnormalities. To these manifestations are added turgor of the tissues, with fluid retention and gain in weight of 1,000 to 1,500 grammes, vasomotor phenomena such as acrocyanosis, and other symptoms such as dermatoses, anginal pain, oedema of the vocal cords and iridocyclitis.

On the basis of the author's ideas on the aetiology of this syndrome an oral complex has been devised for treatment. This consists of the following:

Ammonium chloride ..	300 mg.
Choline theophyllinate ..	100 mg.
Vitamin A	30,000 International Units
Homatropine methylbromide	0·5 mg.

To this is added:

1-p-Chlorphenyl-1-(2 pyrydo)-3-dimethyl-amino-propano maleate	3 mg.
Reserpine	0·2 mg.

It is claimed that this preparation combines the diuretic effect of ammonium chloride with the inhibition of posterior pituitary hormone by choline. Vitamin A is believed to influence the inactivation of oestrogen and maintain the equilibrium of the sex hormones. Homatropine is believed through its anticholinergic action to relieve the physical and psychological tension of the premenstrual syndrome. The antihistamine is believed to

counter the allergic factor in the syndrome while the reserpine acts as a "tranquillizer". Treatment is given thrice daily during the two weeks before menstruation.

A series of 46 patients received this treatment. All were cured after two months treatment and their symptoms were relieved for a further two months after cessation of treatment. Treatment was most successful in dealing with nervous lability, mastalgia, oedema and abdominal symptoms.

[A great deal has been written about pre-menstrual tension since the syndrome was first described over 25 years ago by Novak and Frank. The present work does not advance knowledge of the syndrome or its treatment, though good results are claimed by means of what may fairly be described as "blunderbuss" methods.]

Josephine Barnes

188. **The Cervix and Uterus in Sterility.**

By S. H. STURGIS. *Fertil. Steril.*, **7**, 468–484. Sept.–Oct. 1956.

The pH of vaginal and cervical secretions must play a role in fertility for sperms do not survive in any *in vitro* medium with an acidity equal to that found normally in the vagina. In nature such acidity should be neutralized by the alkaline semen and also by the cervical mucus which runs down into the posterior fornix. The problem of the Sims-Huhner Test is whether the sperms found represent those that are trapped, or do they picture but a fraction of a vigorous population which has already migrated into the uterus. The author considers that "purposeful motion" of the sperms seen in the cervical mucus is the most important thing, but it is difficult to evaluate those cases where after 12 hours the test is poor. He considers that the post-coital test is the best yardstick that we possess, though the degree of *Spinnbarkeit* (2–4 inches) and the degree of fern patterning at the time of ovulation are of imperative importance. Should the cervical mucus be inadequate or hostile he advocates that ethinyl oestradiol ·01–·02 mg. should be given for the first 12 days of the cycle. He is not convinced that suppositories of aureomycin and the like are of great utility for supposed infections of the cervix, though many will agree that penicillin, locally or parenterally is beneficial.

V. B. Green-Armytage

189. **The Ovum in Infertility, Abortion, and Developmental Anomaly.**

By L. B. SHETTLES. *Fertil. Steril.*, **7**, 561–572. Nov.–Dec. 1956.

The author is convinced that the commonest cause of abortion is a defective ovum, spermatozoon, or both. He emphasizes the fact that ovulation can only occur when the ovum has reached a certain maturity which is dependent upon the two gonadotrophic hormones of the anterior pituitary, which must be in exact quantitative proportions. It is well to bear in mind that the follicle at mid-cycle may contain an ovum with degenerative changes quite incompatible with fertilization, and that the number of possibly good ova becomes less and less so with increase in age, particularly after 30. In a study of 1,000 abortions Hertig attributed 62 per cent to defective ova, but he is very sceptical of any therapy for patients who give a history of habitual abortion, particularly therapy of the hormonal type, for the outcome of a given pregnancy is established once for all, at its very beginning, unless of course there is some uterine abnormality or toxic agent present.

V. B. Green-Armytage

190. **Oligospermia: A Clinical Study with Methylandrostenediol.**

By J. M. SCHULTZ. *Fertil. Steril.*, **7**, 523–539. Nov.–Dec. 1956.

Neither blockage of excretory ducts nor fibrosis of the testes is considered in this paper, but rather those far more common cases in which the sperm counts range from a very few to 40 million per ml. At the Sloane Hospital Sterility Clinic, it would appear that all patients with seminal counts under 60 million per ml. are classified as having oligospermia. Thirty-two cases of male infertility were fully investigated. Twenty-eight of these patients suffered from oligospermia, the result of either a reduced rate or retardation of spermatogenesis. Dr. Schultz prescribes 50 mg. of methylandrostenediol by mouth for 8 weeks. He states that there is an increase in actual sperm numbers, motility and libido in the majority. Six pregnancies are reported. *V. B. Green-Armytage*

191. **Influence of Antibiotics on the Motility of Spermatozoa.**

By C. A. JOEL and S. KORNHAUSER. *Fertil. Steril.*, **7**, 430–439. Sept.-Oct. 1956.

This is an interesting paper, for the authors show that pessaries of penicillin and chloromycetin have a definite effect in increasing and prolonging sperm motility, the optimum amount of penicillin being 60,000 units and that of chloramphenicol being 10 mg., whereas other antibiotics cause depression. They give an easy test for discovering the vitality of the spermatozoa. This consists of adding one drop of 1 per cent bluish eosin to a drop of semen. Living sperms remain colourless; immobile or dead ones taking up the stain.

[Such a simple test is perhaps worth knowing. The reviewer is grateful for the reminder that the discovery of human spermatozoa was made by Johann Hamm in 1677, and that this fact was conveyed to the Royal Society of London by the famous Dr. Leeuwenhoek in that year.]

V. B. Green-Armytage

INFECTIONS OF THE REPRODUCTIVE ORGANS

192. **Treatment of Monilial Vaginitis: A Clinical Trial of Nystatin.**

By R. F. JENNISON and J. D. LLYWELYN-JONES. *Brit. med. J.*, **1**, 145–146. Jan. 19, 1957. 4 tables. 12 refs.

Fifty-three women suffering from monilial vaginitis were treated with nystatin pessaries and the results were compared with those obtained by treating 36 similarly affected women with an aqueous solution of gentian violet.

Treatment consisted in the insertion of 2 pessaries containing 100,000 units of nystatin or in painting out the vagina with 1 per cent aqueous gentian violet on 3 alternate days. After a week all the patients were re-examined and in the case of a negative swab being obtained they were asked to attend again one month later. If candida was present on either occasion, treatment was continued for a further week.

Forty-seven (88 per cent) of the women treated with nystatin were free from infection one week after treatment, whereas only 17 (47 per cent) were cured after painting with gentian violet. Four weeks after treatment, the relapse rate in the first group was 21 per cent compared with 46 per cent in the control group. Of 18 cases which failed to respond to gentian violet, 16 were cured with nystatin. One patient was successfully treated with oral nystatin alone.

Nystatin acts mainly on fungi and yeasts and interferes but little with the normal flora of the vagina. Besides being more effective than gentian violet, it has the advantage of not staining linen, etc. Self administration by the patient is easy.

R. W. Grayburn

193. **Gynecologic Aspects of Leprosy.**

By B. E. Bonar and A. S. Rabson. *Obstet. Gynec.*, **9**, 33–43. Jan. 1957. 6 figs. 13 refs.

The authors describe a case of leprous cervicitis, metritis, salpingitis and oöphoritis. Involvement of the female genital organs by leprosy is extremely rare, but the authors give their impressions from a survey of what is known about it. Fertility is rarely affected and menstrual irregularities are uncommon unless there is marked ovarian involvement. Leprous vulvitis occurs infrequently and the vaginal mucosa is rarely involved. Cervicitis in which lepra cells are found has been described, as have endometritis, myometritis and salpingitis. The most commonly involved site is the ovary, which may be involved in repeated leprous infection.

J. G. Dumoulin

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

194. **Quantitative Chorionic Gonadotrophin: Prognostic Value in Hydatidiform Mole and Chorionepithelioma.**

By E. Delfs. *Obstet. Gynec.*, **9**, 1–24. Jan. 1957. 3 tables. 18 figs. 20 refs.

The author has investigated the concentration of chorionic gonadotrophin in the blood serum in 90 cases of hydatidiform mole and 12 of chorionepithelioma. A dried precipitate is made from the serum, suspended in saline and injected into immature female rats. The uterus is excised from the rats, weighed, and compared with the dosage-response curve for the International Standard. It is stressed that the results obtained by this method are more accurate than tests on urine for gonadotrophin.

The serum gonadotrophin levels in normal pregnancy have been previously estimated and reported on by the author and his colleagues.[1] A peak is reached about the 60th day of pregnancy. There is a marked fall after the 85th day. Therefore, attempts to diagnose hydatidiform mole by this method before about the 100th day of pregnancy are useless. A high reading after this time indicates abnormality, and 18 cases of mole were diagnosed in this way before any tissue was passed. A degenerating or dying mole may, however, give a low bioassay reading. Multiple pregnancy can give a high reading, but repeat tests for 2 or 3 weeks will show a fall, following the normal pregnancy curve although delayed. In 88 cases, a mole was suspected but could be ruled out on the finding of normal or low gonadotrophin levels, the conclusion being correct in each case.

Gonadotrophin tends to appear in the spinal fluid in small amounts when the serum level is high for any reason.

Follow-up studies were made in 90 cases of hydatidiform mole. Individual behaviour varied between a rapid and slow disappearance of gonadotrophin in the serum. In a few cases where the disappearance was slow repeat curettage yielded mole fragments. In 5 cases a new pregnancy supervened during the follow-up and was recognized by the normal pregnancy curve. In 19 cases, positive assays were present after 60 days: ten continued with decreasing levels. Eight had a hysterectomy performed because of their dubious clinical state. Five of these were classified as having invasive moles; 1 or 2 were dying moles and probably would have caused no difficulty had they been left; 1 of the 5 persisted as a histologically benign but metastasizing growth and proved fatal. Three patients developed chorionepithelioma.

Of the 9 cases in the series of 90 who had an initial hysterectomy as treatment of the mole, 1 developed fatal chorionepithelioma.

From experience with these cases, the author advises the following plan: Thorough curettage should be carried out in the puerperium: contraception should be used during the follow-up period to avoid confusion. Quantitative assays of the serum should be made at 2-week intervals at first, and then 3–4 week intervals until negative. If the serum gonadotrophin is over 20,000 I.U./litre after 30 days or shows a rising titre, if there is bleeding or subinvolution, a second curettage is indicated followed by weekly serum assays. If the level then rises or remains high, hysterectomy should be carried out. Assays should be continued, and if positive results are persistently found, metastases should be looked for.

Serum tests in a further 8 cases of chorionepithelioma are briefly reported in the series.

J. G. Dumoulin

195. **The Treatment of Carcinoma of the Corpus Uteri.**

By B. C. Murless. *S. Afr. med. J.*, **31**, 120–124. Feb. 9, 1957. 1 fig. 24 refs.

Many cases of carcinoma of the body of the uterus are treated today as they were 50 years ago, except for the addition of radiotherapy by some surgeons. The author claims that this is insufficient and that a more radical approach is justified. Methods of treatment (surgery

alone, radiation alone, surgery and post-operative radiation, surgery and pre-operative radiation, and vaginal hysterectomy) are listed. Truly comparative results are difficult to obtain. Absolute 5-year survival rates reported by many clinics are 55–60 per cent. Almost 20 per cent of the survivors die before the 10th year. The author thinks that dangerous complacency exists in our management of this condition.

Recurrences in the vagina or pelvic lymph nodes, or as a pelvic mass are discussed. Lymph nodes are involved in 7–28 per cent of cases. Lymph drainage is described, the uterus being divided into upper, middle and lower thirds designated 1, 2 and 3 respectively.

The author dismisses hysterography and fractional curettage as inaccurate methods for demonstrating the position of the growth. The latter method is useful for demonstrating endocervical carcinoma. It is suggested that examination of the cut uterus is accurate, and post-operative staging is suggested (stage 1 involving area 1, stage 2 involving areas 2 and 3, and stage 3 being spread beyond the uterus or pelvic lymph node involvement).

Shortcomings of the previously listed methods of treatment are described. For the past 6 years the author has treated carcinoma of the body by Wertheim's hysterectomy, with the addition in the last 4 years of pre-operative radiation. A single Stockholm application is employed 2 weeks prior to operation. At operation the cervix is occluded by suture after plugging with gauze soaked in iodine. Wertheim's hysterectomy is performed and the upper one-third of the vagina is removed. The uterus is opened and inspected. The lymph nodes are removed in all cases, except where a small growth is confined to area 1 in old patients where conditions suggest that the additional trauma might be dangerous.

Five-year figures for this form of treatment are as yet few. The author claims that operability rates should be high, as age and obesity are not contra-indications to radical surgery. Generally if a patient is fit for hysterectomy she is fit too for Wertheim's hysterectomy. Operability rates quoted vary between 87·4 per cent and 95 per cent. Pulmonary embolism still remains the greatest hazard.

The writer submits that the time has come to "unteach" the established dogma that total hysterectomy with removal of tubes and ovaries is the treatment of choice in carcinoma of the body.

L. J. Abramowitz

196. **Mixed Mesodermal Tumour of the Cervix.** (Tumeur mésodermique mixte du col utérin.)

By P. Potvliege and M. Petit. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 638–650. 1956. 5 figs. 36 refs.

A mixed mesodermal tumour of the uterine cervix was observed in a 28-years-old patient. Histologically it was characterized by the presence of rhabdomyoblasts surrounded by myxomatous stroma. The tumour recurred locally several times after incomplete removals. A total hysterectomy was carried out; ten months afterwards no signs of recurrence have been noted.

The histological structure of mixed mesodermal tumours, their histogenesis, their localization, their clinical features and the problem of their malignancy, are discussed. It must be emphasized that these tumours, which are to be considered malignant, are at first localized, and at this stage both clinical and histological diagnosis may be erroneous.

From the Authors' Abstract

197. **Historical Survey of Methods of Classification of Carcinoma of the Cervix Uteri.** (Sviluppo storico-clinico della classificazione del cancro del collo dell'utero.)

By G. Hecht-Lucari and F. Jenkner. *Ann. Ostet. Ginec.*, **78**, 505–534. 1956. 96 refs.

A historical survey is given of methods of classification of carcinoma of the cervix from 1899 to 1955. These methods fall into three classes; those based on operability, those based on clinical findings and those based on operative and clinical findings. A total of 57 different classifications have been found in the literature and these are individually summarized. Most of those since 1929 have been based on the League of Nations Cancer Commission.

These classifications are discussed in relation to carcinoma *in situ* and also in relation to new views reached as a result of modern operative techniques.

Josephine Barnes

198. **Endomitotic Nuclear Growth in a Human Cervical Carcinoma.**

By S. Timonen and E. Therman. *Ann. chir. gynaec. fenn.*, **45**, 237–244. 1956. 4 figs. 13 refs.

The metaphase/prophase index is said to increase with the anaplasia of a tumour. A case of carcinoma of the cervix is described where squash preparations of the biopsy have been exhaustively examined. The metaphase/prophase index was 1·52 and the growth was exceptional in that there were numerous giant cells present the growth of whose nuclei had occurred through endomitosis.

D. M. Sheppard

199. **A New Radium Applicator for the Treatment of Cervical Cancer.**

By A. Saloheimo. *Ann. chir. gynaec. fenn.*, **45**, 264–269, 1956. 2 figs. 15 refs.

The chief complications following radium treatment of carcinoma of the cervix are due to excessive irradiation of bladder and rectum. The author describes an apparatus, built on the lines of the blade of a Sims' speculum, for the application of radium to the cervix and parametrium. This apparatus diminishes irradiation of bladder and rectum and holds the radium firmly fixed against the cervix. It seems worthy of trial and is manufactured by Instrumentarium O/Y, Helsinki.

D. M. Sheppard

200. **The Problem of Pre-invasive Carcinoma of the Cervix.** (Le problème du cancer préinvasif du col utérin.)

By T. Antoine. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 622–629. 1956. 10 refs.

After considering pre-invasive cervical carcinoma as a

pathological entity and emphasizing the diagnostic difficulties, the author reports his management of this lesion.

From the Author's Abstract

201. **Carcinoma in Situ.**

By H. R. FISHER. *West. J. Surg. Obstet. Gynec.*, **64**, 630–637. Dec. 1956. 19 refs. 8 figs.

The term carcinoma *in situ* is limited to intra-epithelial carcinoma, and the author, Professor of Pathology in the University of Southern California, points out that it occurs in many sites other than the uterine cervix. In the cervix the lesion looks benign but in the larynx, skin, stomach and gall bladder there are definite alterations in the epithelium, the changes being summarized as localized oedema or thickening with congestion; hyperkeratosis and leukoplakia should also be suspect. The incidence of the lesion is still hard to evaluate but the age distribution is as wide as that of invasive carcinoma but some years younger. The diagnosis rests entirely on the pathologist and it is a difficult matter to formulate specific criteria. The histological features are lack of differentiation, altered epithelial pattern with alteration of the polarity of cellular orientation, hypercellularity, cellular atypism, altered staining reactions and mitoses. The biological features of the condition are discussed and the author does not think that the condition is reversible. If evidence of the condition is found it should not be regarded as a final diagnosis but extensive search made for possible co-existing invasive carcinoma. The author concludes that the recent trend towards conservative treatment should be completely justifiable on the basis of all that is known at present about the disease.

[This is a most interesting paper as it gives a wide view of this condition.]

D. C. A. Bevis

202. **Nuclear Pyknosis of Vaginal Cells. Critical Study of Various Criteria. Need for an Exact and Standardized Definition.** (La pycnose nucléaire des cellules vaginales. Etude critique des différents critères. Nécessité d'une définition précise et standardisée.)

By J. P. PUNDEL and C. LICHTFUS. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 630–637. 1956. 1 table. 2 figs. 7 refs.

In 50 vaginal smears, the karyopyknotic index was determined in four different ways: by ordinary microscopy and subjective evaluation, by phase contrast microscopy, by tinctorial evaluation, and by immersion microscopy and precise micrometric evaluation taking 6 μ as maximal nuclear diameter.

The comparison of the different results thus obtained with four different methods in evaluating a total of 15,000 nuclei showed that the determination of the karyopyknotic index of vaginal smears may give very variable results depending on the criterion used, and also that no definite relation exists between the results obtained by means of these four different procedures. It is therefore absolutely necessary, that every cytologist reports the criteria in detail which served to determine the karyopyknotic index figures. Only by doing so, will it become possible to compare research results of different authors and to avoid useless controversy. In current practice, phase-contrast microscopy is the recommended procedure for evaluation of pyknosis in a coloured smear. In the first place, the index thus obtained corresponds fairly well to the one found by precisely measuring the nuclei taking 6 μ as maximal diameter, and on the other hand those two index figures closely follow the oestrogenic stimulation.

From the Authors' Abstract

203. **Adrenal-like Tumor of the Ovary (Masculinovoblastoma).**

By J. P. PALMER and G. M. WALDROP. *Obstet. Gynec.*, **9**, 44–47. Jan. 1957. 3 figs. 9 refs.

A case of masculinovoblastoma, thought to be the 27th reported in the English-language literature is described. The patient was markedly obese, hirsute and hypertensive, and removal of the tumour improved her considerably. *J. G. Dumoulin*

204. **Mesonephric Carcinoma of the Ovary: Report of a Case.**

By H. E. BOWLES and I. L. TILDEN. *Obstet. Gynec.*, **9**, 64–70. Jan. 1957. 9 figs. 22 refs.

A partly cystic partly solid ovarian tumour was removed from a 52-year-old patient. The solid part was identical in microscopic appearance to a clear-cell carcinoma of the kidney. In addition there was a definite tubular and papillary pattern in many areas, similar to a mesonephroma. The patient is well with no evidence of recurrence 4 years after surgery and post-operative irradiation. *J. G. Dumoulin*

205. **Primary Ovarian Carcinoma.**

By G. J. CARLIN and R. J. FRODEY. *Obstet. Gynec.*, **9**, 71–76. Jan. 1957. 12 tables. 10 refs.

Between 1921 and 1950, 133 primary carcinomas of the ovary were operated on by the authors. The highest incidence was between the ages 35 and 65. The commonest symptoms were pain and abdominal swelling.

Laparotomy only was carried out in 45 cases, hysterectomy with removal of adnexa in 38 cases, bilateral salpingo-oöphorectomy only in 30 cases and unilateral salpingo-oöphorectomy in 20 cases.

The 5-year survival rate was 23·3 per cent and 10-year survival rate 18·5 per cent.

Treatment should consist of total removal of uterus, tubes, ovaries and omentum followed by radiation therapy. With extensive pelvic involvement and incomplete removal of the tumour, bilateral salpingo-oöphorectomy should be performed and the uterus left for radium and deep therapy.

J. G. Dumoulin

OPERATIONS

206. **A New Instrument for Hysterosalpingography.**

By C.-E. JOHANSON. *Ann. chir. gynaec. fenn.*, **45**, 245–249. 1956. 5 refs.

The author discusses the technical difficulties of hysterosalpingography. He describes an instrument for use in this technique which differs from the ones in common use in that it has a flexible tip. This appears to be advantageous in certain circumstances.

D. M. Sheppard

207. **The Use of Short-acting Intravenous Anaesthetics in Clinical Gynaecology.** (L'utilisation des anesthésiques intraveineux à action ultra-courte en clinique gynécologique.)

By M. THIERY. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **26**, 611–613. 1956.

The author reports the results obtained in the Gynaecological Department, State University, Ghent, with a short-acting intravenous anaesthetic.

From the Author's Abstract

208. **Extra-genital Operations in the Course of Gynaecological Surgical Practice.** (Chirurgia extragenitale complementare e necessitatis nel corso di interventi ginecologici.)

By P. N. SILIQUINI and G. PINOLI. *Ann. Ostet. Ginec.*, **78**, 535–574. 1956. 12 figs. 166 refs.

A review is given of 729 paragynaecological and extragenital operations undertaken in a total of 4,060 gynaecological operations, or 17·8 per cent of the total. These included the following:

Operations on the abdominal parietes, including herniotomies, 22 cases.
Closure of an intestinal fistula, 1 case.
Operations on the intestines, 648 cases.
Mesenteric cyst, 1 case.
Appendicectomy was performed in 625 cases.
Haemorrhoidectomy was performed alone in 12 cases and with other procedures in 10.

Operations on the urinary tract included exenterations, total and anterior and posterior; also ureteric anastomoses, end to end, into the skin and into the bowel.

There was one case of paravesical fibroma.

Resection of the pre-sacral plexus was performed for various indications in 49 cases. *Josephine Barnes*

209. **Congenital Absence of the Vagina.**

By N. F. MILLER and W. STOUT. *Obstet. Gynec.*, **9**, 48–54. Jan. 1957. 6 tables. 4 refs.

Corrective measures in cases of congenital absence of the vagina such as the Baldwin-Schubert operation are very rarely necessary today. For most cases the treatment consists of dissecting a channel between the bladder and rectum and insertion of a skin-graft covered obturator. Generally, a split-thickness skin graft taken from the thigh is used. Some surgeons dissect a channel and insert an obturator without skin graft. In both instances the obturator must be worn for 3 or more months.

The authors have treated 54 cases, 46 with a graft and 8 by dissection of a channel only. An occasional operative complication is a vesico-vaginal or recto-vaginal fistula. The best time for doing the operation is the late teenage. On the whole the operative results were satisfactory, and of those who got married the majority of cases could have intercourse successfully.

J. G. Dumoulin

210. **Experience With the Manchester Operation.**

By E. C. HILL and R. W. HOAG. *Surg. Gynec. Obstet.*, **104**, 167–175. Feb. 1957. 2 figs. 8 tables. 6 refs.

This is a report from the University of California Hospital, San Francisco, of 15-years experience of the Manchester operation in the treatment of genital prolapse. The material consists of 505 operations performed during the period 1937–1951. In 69·5 per cent of the cases uterine descent was present. The operation was also employed for cases without a significant degree of prolapse but with cystocele or rectocele and cervical lacerations with chronic cervicitis.

The mortality rate was 0·4 per cent and the morbidity rate 32·7 per cent. Urinary tract infection was by far the most common post-operative complication. In 4 cases unsuspected early squamous cell carcinoma of the cervix was found on microscopic examination of the amputated cervix.

Five per cent of patients developed subsequent disease involving the uterus of sufficient degree to require additional treatment. No patient developed carcinoma in the remaining portion of the cervix. The incidence of malignant disease involving the corpus following the operation was 0·4 per cent, which is not considered of sufficient significance to warrant prophylactic vaginal hysterectomy.

Seventeen pregnancies are known to have occurred in 15 cases following the Manchester operation. There was no evidence that the operation affected materially the course of pregnancy. Of those delivered per vaginam, a very high proportion had subsequent pelvic floor relaxation of varying degree but this did not follow in those delivered by elective Caesarean section.

It was found that follow-up examinations within a year of operation produced results which were not valid. In those patients followed for more than 1 year, 78·9 per cent remained free from symptoms and the operation was anatomically satisfactory in 66·8 per cent.

The authors conclude that at the University of California Hospital the Manchester operation has proved to be an effective procedure in the treatment of genital prolapse. *John P. Erskine*

211. **Functional Disturbances of Bladder and Ureter Following Wertheim Operations.** (Über Funktionsstörungen von Ureter und Blase nach der Wertheimschen Operation.)

By O. BUSSE and H. MUTH. *Zbl. Gynäk.*, **79**, 114–127. Jan. 19, 1957. 6 figs. 19 refs.

With the reduction of the mortality due to this operation, disturbances of normal function of the urinary tract have gained increasing importance.

The authors have made it practice to examine urologically all patients on whom this operation was carried out. They report the results in 170 women free from recurrence out of a total of 280 cases. The investi-

gations reported are not concerned with post-operative ureteric fistulae (25 cases=8·9 per cent) almost all secondary to necrosis. Urological investigations in each case included cystoscopy, indigo-carmine test, measuring of intra-vesical pressure and tone of the sphincter, estimation of any residual urine and minimal and maximal capacity. Intravenous pyelography was carried out in all cases in which the indigo-carmine efflux was atypical.

Spontaneous micturition usually set in between the 18th and 20th post-operative days. The average time by which the patients were free from residual urine was 23 days after operation, but in 2 patients it took over 100 days. Of the 170 patients followed up, difficulty of micturition was a complaint in 42 per cent during the first year and in 16 per cent after that period. Absence of desire to micturate occurred in 36 per cent following the operation and decreased to 13 per cent after a year. The authors were impressed by the relatively common post-operative sphincteric insufficiency manifested by incontinence in 16 per cent of patients during the first year. The incidence decreased after a year to 5·7 per cent. This symptom is attributable to a mechanical cause resulting from cicatricial traction, whereas the other symptoms previously mentioned are probably due to denervation of the bladder in the course of the extensive operation.

The observations show that the 3 symptoms were largely reversible and subsided within the first post-operative year in two-thirds of their cases.

In the course of 228 cystoscopies 30–100 ml. of residual urine were found in 17 per cent of cases one year after operation, although all these patients had no residual urine at the time of their original discharge from hospital. The majority of patients reported a sense of fullness with 250–300 ml. of fluid in the bladder, but in almost all patients the bladder capacity increased above the pre-operative amount. Trabeculation was observed in 34 per cent of patients, due to post-operative bladder hypertrophy. The indigo-carmine test was normal in 128 of the 170 patients whereas in 42 (25 per cent) there was abnormal efflux on one or both sides. Of this group 28 (16 per cent of the 170) patients showed on further investigation varying degrees of functional or organic abnormalities such as hydro-ureters, hydronephrosis and in some cases pyonephrosis. These lesions are probably due to cicatricial ureteric stenosis. The resulting hydronephrosis may lead to suppression of renal function (5 cases) or recurrent pyelitis and pyonephrosis (2 cases). Contributory factors may have been post-operative X-ray therapy, post-operative atony of the ureter and fibrosis of the vesical sphincter.

In 11 patients spontaneous improvement or complete regression of hydronephrosis could be observed, but re-implantation of the ureter was required in 2 and nephrectomy in 5 patients.

If the 25 ureteric fistulae are included, serious functional or organic derangement of the urinary tract was found in 18·9 per cent. The figure may even be higher if it is considered that only 170 out of 280 patients were examined.

The authors emphasize the relatively symptomless progress of serious changes in the urinary tract subsequent to Wertheim operation and advised routine urological follow-up examinations. *Bruce Eton*

212. **Method of Avoiding Ureteric Fistulae Following Radical Vaginal Hysterectomy.** (Eine Methode zur Vermeidung der Ureterfisteln bei der vaginalen Radikaloperation.)

By R. HORN. *Zbl. Gynäk.*, **79**, 112–114. Jan. 19, 1957. 1 fig.

During dissection of the ureter on the side of the uterus the bladder pillar is left attached to the uterus, the bend in the ureter is freed around its whole circumference and the uterine vessels are exposed. A thin rubber drain 60–70 cm. long is passed behind the ureter and the two ends are held up by the second assistant during further dissection in the region of the ureter. This results in slight tension between ureter and parametrium so that the ureter can be dissected further under clear vision. It is freed only posteriorly so that the lateral and anterior tissues maintain an adequate blood supply to the wall of the ureter. This allows a wide resection of the parametrium as far as the lateral pelvic wall.

The author has used this method in 150 patients without a single case of ureteric fistula. *Bruce Eton*

213. **The Effect of Radical Gynaecological Operations on Renal Clearance.** (Die Nieren-Clearance bei gynäkologischen Radikaloperationen.)

By W. HELBING. *Zbl. Gynäk.*, **79**, 85–106. Jan. 19, 1957. 11 figs. 80 refs.

The creatinine clearance was estimated in 3 groups of patients before, during and after radical (mostly vaginal) operations for carcinoma cervicis uteri, carried out under epidural anaesthesia. The operating time ranged from 60 to 100 minutes. Half-way through the operation a blood transfusion was given routinely. The series includes 40 patients.

In the first group of 20 patients, 15 had vaginal and 5 abdominal operations. Creatinine clearance during operation showed very low values. In the second group, 14 cases were therefore investigated during the day of operation and these showed a marked reduction of clearance at the time of operation. In the third group simultaneous estimation of glomerular filtrate (by creatinine clearance) and renal plasma flow (using "Nephrotest") were carried out in 6 patients.

All cases showed a drop in clearance values during operation, whether vaginal or abdominal, which rose again subsequently and reached normal figures after variable intervals. In 4 cases, values never dropped below the normal range (70–170). In 6 patients it fell below the normal range during operation but improved in the second half of the operation during which blood transfusion was given.

In 5 patients creatinine clearance decreased to extremely low levels (less than 10) during operation. It is of interest that the lowest values occurred in 3 Wertheim operations (0, 0, 3, respectively) but even in these the clearance values rose during the second half

of the operating time. The fact that in 5 patients the lowest values occurred while the transfusion was actually in progress is regarded by the author as evidence that the rise observed in the other patients is not due to transfusion.

In the author's experience the average renal plasma flow in women was 659 ml./minute. The renal plasma flow was reduced at the same time as the glomerular filtrate.

In contrast to what might be expected, the author did not find any correlation between creatinine clearance values and the patient's blood pressure. This is attributed to the fact that circulatory failure as seen in cases of shock was absent during operation, although there was temporary hypotension.

He considers that the reduction in renal function during operation is not due to blood or fluid loss, because even if infusions were started before operation the drop in clearance values could not be prevented.

The circulatory changes in the kidneys during operation are not a response to fluid loss but to surgical trauma. This probably causes a nervous reflex resulting possibly in a Trueta shunt (spasm of interlobular arteries), but the finding of an increased filtration fraction (ratio of volume of glomerular filtrate/plasma flow) was suggestive of increased contraction of the vasa efferentia of the glomeruli.

Pituitary anti-diuretic hormone and A.C.T.H. may play a part in restoring normal renal function but are not necessary for an explanation of its impairment.

There may be a relationship between the renal changes observed during operation and post-operative anuria caused by shock.

Bruce Eton

UROLOGY

214. Urinary Incontinence.

By A. A. MARCHETTI. *J. Amer. med. Ass.*, **162**, 1366–1368. Dec. 8, 1956. 2 refs.

The author presents some further observations upon the operation of vesico-urethral suspension, which he first described with Marshall and Krantz in 1949. While the unfailing cure for stress incontinence has yet to be found, of 132 patients who had a simple vesico-urethral suspension, 84 per cent were considered completely cured.

As a preliminary to selection of cases full urinary investigation must be carried out, especially urine culture and endocystoscopy. A few minor modifications have been made to the original technique. The use of the assistant's fingers in the vagina is no longer considered necessary, and the main sutures are now placed deeply into the vaginal wall adjacent to the urethra, but not to include the lateral wall of the urethra.

Transient haematuria may be expected in about 75 per cent of cases for the first 24 hours after operation. Four cases of periostitis pubis were noted in this series but all responded to antibiotic therapy. Repeated catheterization was necessary in four patients up to 17 days after operation, and cellulitis around the incision occurred twice. One urinary fistula occurred in a case where non-absorbable suture material was used, but this healed spontaneously in three weeks. The only death in this series was from pulmonary embolus in a woman 75 years of age. The operation is chiefly recommended after previous vaginal approach has failed.

D. W. James

NOTICES

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The Editor is: Professor James Young, *D.S.O.*, M.D., F.R.C.S., F.R.C.O.G., Paynes Hill House, Steeple Aston, Oxford.

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Brown, H. E., and Jones, B. K. (1943): *J. Obstet. Gynaec. Brit. Emp.*, **2**, 128.

Sampson, P. (1940): *Obstetrics for Midwives*. 2nd edition. Fraser, London. p. 9.

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